No. 16-1378

IN THE

United States Court of Appeals for the Federal Circuit

IN RE: DEPOMED, INC.,

Appellant,

Appeal from the United States Patent Trial and Appeal Board in IPR No. 2014-00652

NON-CONFIDENTIAL OPENING BRIEF FOR APPELLANT

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Dated: April 29, 2016

CERTIFICATE OF INTEREST

Pursuant to Federal Circuit Rule 47.4, counsel for Depomed, Inc. certifies the following:

1. The full name of every party represented by me is: Depomed, Inc.

2. The real party in interest represented by me is: N/A

3. All parent corporations and any publicly held companies that own 10% or more of the stock of the parties I represent are as follows:

Depomed, Inc. has no parent corporation and no entity owns more than 10% of Depomed, Inc. stock.

4. The names of all law firms and partners or associates that appeared for the parties represented by me in the trial court or that are expected to appear in this court are: Hogan Lovells US LLP: Arlene L. Chow, Eric J. Lobenfeld, Peter H. Noh, Ernest Yakob, Jessica L. Ellsworth, Jaclyn L. DiLauro, Thomas P. Schmidt.

Dated: April 29, 2016

/s/ Arlene L. Chow
Arlene L. Chow

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CONFIDENTIAL MATERIAL OMITTED

The material omitted in this brief relates to profits from licensing and collaborative agreements using the ’340 patent’s technology as well as the number and growth of prescriptions written for Gralise, a drug that incorporated the ’340 patent’s technology. That material is confidential and subject to a protective order in the Patent Trial and Appeal Board.

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STATEMENT OF RELATED CASES

Pursuant to Federal Circuit Rule 47.5, counsel for Appellant Depomed, Inc. states that no other appeal from this *inter partes* review proceeding was previously before this Court, or any other court. Two cases, one now and one soon-to-be pending before the Supreme Court of the United States, could directly affect this Court's decision in the pending appeal because they address the constitutionality of the Patent Trial and Appeal Board's *inter partes* review procedure. *See Cooper v. Lee*, No. 15-955 (docketed Jan. 28, 2016); *MCM Portfolio LLC v. Hewlett-Packard Co.*, No. 15A872 (filed Feb. 18, 2016) (application to extend the time to file a petition for a writ of certiorari granted until April 29, 2016).

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JURISDICTION

Depomed, Inc. (Depomed) appeals from a final judgment of the U.S. Patent Trial and Appeal Board (PTAB or Board), entered on September 16, 2015. *See* Appx1-43. The PTAB had jurisdiction under 35 U.S.C. § 311. Depomed filed a timely notice of appeal on November 13, 2015. *See* 28 U.S.C. § 2107; Fed. R. App. P. 4(a); Fed. Cir. R. 4; Appx44-48. This Court has exclusive jurisdiction under 28 U.S.C. § 1295(a)(4)(A).

INTRODUCTION

Administering an oral drug is more complex than choosing a medication and an amount. In particular, there are many ways to change how a body *absorbs* a drug once it is swallowed that can be crucial to successful therapy. Take

gabapentin, for instance, which is used to treat nerve pain for patients with post-herpetic neuralgia. When given in an "immediate-release" formulation, a patient would take it in high doses multiple times a day, which can lead to bad side effects and complications. A better formulation would be taken once a day and then retained in the stomach, with the drug released slowly and evenly over time. But such a formulation—called a "gastric-retentive, controlled-release formulation"—was challenging to develop because of the restricted way in which gabapentin is absorbed in the body.

Depomed, Inc. took on—and met—that challenge. It invented a unique polymer combination that provides both gastric retention and controlled release of an oral medication. Before the invention described in U.S. Patent No. 6,723,340—"Optimal Polymer Mixtures for Gastric Retentive Tablets" ('340 patent)— there had long been a need for this sort of dosing formulation for challenging drugs like gabapentin. But no one had combined polyethylene oxide (PEO) and hydroxypropyl methylcellulose (HPMC) for this purpose. *See* Appx49-60 (patent). In fact, the PEO-HPMC polymer combination tablet had unexpectedly surprising characteristics: It provided *better* controlled-release properties than a tablet made of either polymer individually *and* it mitigated the undesirable qualities of a tablet consisting of either polymer alone.

Finding a polymer combination that could achieve the results described in the '340 patent was far from simple. "The goals of gastric retention and controlled release are not always compatible." Appx55 at 3:10-11. For example, although PEO has desirable controlled-release properties and swells extremely well—which is useful for gastric retention—it has to be used at high levels to deliver high doses of drugs. But there were serious concerns about whether high levels of PEO can clear quickly enough from the gastrointestinal tract. Appx627 at ¶ 40. Indeed, at the time of the invention in the '340 patent, FDA had been critical of using large amounts of PEO in oral, pharmaceutical dosage forms. Appx55 at 3:11-19.

HPMC was also far from ideal when used alone. At the time of the '340 patent's invention, HPMC was used most commonly in the pharmaceutical industry in *erodible* controlled-release dosage forms, not swellable forms—that is, dosage forms which break apart slowly rather than expand. Appx755 at ¶ 22. Indeed, HPMC was criticized as eroding *too* readily, causing a large initial release of drug and the poor control of drug release after that. Appx55 at 3:19-30.

The combination of any two polymers is unpredictable as a general proposition. But given what was known about PEO and HPMC individually, the combination of HPMC and PEO could have resulted in reduced gastric retention or poorer control of drug release. *Id.*; *see* Appx755 at ¶ 23. As part of their search to solve the long-felt need for a gastric-retentive, controlled-release dosage form, the

'340 patent's inventors tried dozens of formulations over many months. Appx751-752. And the results of the PEO-HPMC combination were surprisingly good: mixing PEO with HPMC improved the undesirable characteristics that each polymer has individually; it kept the concentration of PEO low enough to avoid FDA's concern with a toxicological risk while slowing the too-rapid erosion of HPMC. Appx628 at ¶ 44. The combination provided *better* controlled release of a drug than did either polymer standing alone, Appx58 at 9:46-48, 628 at ¶ 43, while also providing exceptional gastric retention and delivering more drug over time than did an immediate-release dosage form. Appx59 at Table 4.2. All of that is spelled out in the patent.

And yet the Board concluded that the '340 patent was invalid as obvious. In reaching that conclusion, the Board committed a series of legal errors, each of which merits reversal. To begin with, the Board ignored the unexpected results of the PEO-HPMC combination even though this Court's precedents make clear that unexpected results counsel against an obviousness conclusion. Then the Board found that there was no "long-felt but unmet need" because no one else had tried and failed to invent the patent's claims even though there is no such "tried and failed" prong to evaluating whether a long-felt need existed. Finally, the Board fell prey to classic hindsight bias by casting aside the unpredictability of polymer combinations in general, and those involving PEO or HPMC in particular.

Compounding those errors, the Board's analysis of the objective considerations of non-obviousness was also flawed. In addition to improperly assessing unexpected results and long-felt need, the Board completely discounted the extensive commercial success and licensing agreements that flowed from the '340 patent's invention.

The Board's declaration of unpatentability should be vacated or reversed.

STATEMENT OF THE ISSUES

1. Whether the PTAB erred in declaring the '340 patent unpatentable for obviousness.

2. Whether *inter partes* review violates Article III and the Seventh Amendment.

STATEMENT OF THE CASE

A. The '340 Patent.

One innovation of modern medicine is that scientists can target a drug to its destination in the body and equip the drug to remain there. By maximizing a drug's efficiency and minimizing its side effects, gastric-retentive, controlled-release drugs provide a number of benefits. Stomach disorders—such as esophageal reflux disease, ulcer-causing bacteria in the gastric mucosa, and disorders that require sustained antacid action—can be treated with fewer side effects and less frequent dosing. And other drugs have their greatest therapeutic

effect when released in the stomach; patients taking those drugs likewise benefit from a formulation that allows for a prolonged, continuous, and controlled release in the stomach and upper gastrointestinal tract.

Although using dosage forms to localize drug treatment is often desirable, developing a gastric-retentive, controlled-release dosage form posed a challenge with respect to certain drugs. As of 2001, the prior art taught that one way of achieving gastric retention was to administer particles that were small enough to be swallowed comfortably but would swell to a size large enough to be retained in the stomach upon contact with the stomach's gastric fluid. The prior art also taught that one way a dosage form could provide controlled release of a drug over time was to place the drug within a polymer matrix that was designed either to have a slow diffusion rate or to erode slowly.

But before the '340 patent, drugmakers struggled to deliver high doses of certain drugs in a gastric-retentive, controlled-release dosage form. Gabapentin exemplifies the problem. It is used to treat post-herpetic neuralgia (nerve pain associated with the shingles virus), and before the '340 patent, it was available only in an immediate-release dosage form that had to be taken three times a day. Appx758-759 at ¶ 32. The immediate-release version involved repeated high doses of gabapentin, which led to dizziness and somnolence, and often greatly impacted the patient's quality of life during the day. *Id.* Those complications

caused patients to skip doses and made the drug less effective for treating post-herpetic neuralgia. *Id.*

But creating a gastric-retentive, controlled-release gabapentin dosage form was problematic. Gabapentin exhibits extremely low absorption in the colon, and higher drug doses do not result in greater absorption. Appx758 at ¶ 32. As a result, a gastric-retentive, controlled-release gabapentin dosage form had to be retained in the stomach for very long periods of time, with a very slow release of the drug. Despite the well-known need for a gastric-retentive, controlled-release dosage form that would deliver high doses of gabapentin slowly, evenly, and reproducibly without the side effects of dizziness and somnolence, it was not available before the '340 patent's priority date. Appx758-759 at ¶¶ 32-34.

Depomed's scientists solved this problem, which was a difficult task. They experimented with more than a dozen polymer classes. Appx751 at ¶ 15. They performed a rigorous battery of tests on each formulation, including drug-release studies, disintegration tests, swelling tests, mechanical-integrity tests, stability of drug tests, and stability of tablet tests. Appx752 at ¶ 16. In many cases, they had to develop the tests before they could perform them—including reliable testing mechanisms to measure swelling and erosion in conditions mimicking those in the stomach. Appx752-753 at ¶ 17-18. All of this testing led Depomed's scientists to discover, to their surprise, that using PEO and HPMC in *combination* could create

a swellable, gastric-retentive, controlled-release tablet that would effectively deliver high doses of problematic drugs such as gabapentin. Appx755-756 at ¶ 24.

There were many reasons the success of this combination was unexpected. Although PEO alone was known to provide gastric-retentive controlled release, it raised regulatory concerns about toxicity when used at the high levels that would be necessary to deliver large doses of a drug: "[T]he amounts needed for sufficient swelling to achieve gastric retention . . . raise[ ] regulatory concerns, since the United States Food and Drug Administration lists [PEO] as a substance with undefined toxicology considerations when used at sufficiently high doses on a long-term basis." Appx55 at 3:14-19. The other polymer used in the invention, HPMC, was known to swell and was not considered a toxicology risk by FDA, but it presented other problems. It swells to a lesser degree than PEO, and it erodes quickly in the gastric environment, causing an initial burst of drug release and poor control of the drug's release over time. *Id.* at 3:19-30.

The inventors found, counterintuitively, that a matrix made of PEO and HPMC would retain the beneficial swelling characteristics of both individual polymers, while slowing the erosion of the HPMC and reducing the necessary levels of PEO to avoid the regulatory concerns about toxicity. Appx628 at ¶ 44; *see also* Appx58 at 9:46-48. The inventors obtained a surprisingly good balance of total swelling (for gastric retention), rate of swelling (to prevent esophageal

blockage) and erosion (for reproducible disintegration of the dosage form). Appx755 at ¶ 24. It also turned out that a matrix combining PEO and HPMC would provide better controlled release of gabapentin than would either polymer standing alone. Appx628 at ¶ 43.

The '340 patent memorializes those unexpected results. Claim 1 recites:

> A controlled-release tablet for releasing a drug into at least a portion of a region defined by the stomach and the upper gastrointestinal tract, said tablet comprising a solid monolithic matrix with said drug dispersed therein, said matrix comprising a combination of poly(ethylene oxide) and hydroxypropyl methylcellulose at a weight ratio that causes said matrix to swell upon contact with gastric fluid to a size large enough to provide gastric retention, wherein;
>
> said drug has a solubility in water that exceeds one part of said drug per ten parts of water, by weight, and wherein;
>
> said poly(ethylene oxide) has a viscosity average molecular weight of from about 2,000,000 to about 10,000,000 daltons, and wherein
>
> said hydroxypropyl methyl cellulose has a viscosity of from about 4,000 centipoise to about 200,000 centipoise, measured as a 2% solution in water.

Appx59 at 11:60-12:9.[1]

This breakthrough in dosage-form matrix formulations, part of Depomed's Acuform® technology, allowed a gastric-retentive, controlled-release gabapentin tablet finally to hit the market. That product—named Gralise®—addressed a long

[1] In addition to claim 1, claims 2-5 and 10-13 were also challenged before the PTAB. Claims 2-5 and 10-13 are all dependent on claim 1.

desired goal to have a gastric-retentive controlled release form of gabapentin, reducing side effects and improving compliance in treating post-herpetic neuralgia. Appx758-759 at ¶¶ 32-33. The invention of the '340 patent also led to a diabetes drug—called Glumetza®—that provides gastric-retentive controlled release of metformin, likewise reducing side effects diabetic patients previously had suffered from immediate-release dosage forms. Appx758 at ¶ 31.

The market responded to this important new technology, and sales of Depomed's Gralise took off. In its first 27 months, doctors wrote more than [redacted] prescriptions. Appx666 ¶ 9, 678-679 at ¶ 32. Gralise vastly outperformed Horizant®, another gabapentinoid drug that launched around the same time without a gastric-retentive, controlled-release formulation. Appx679 at ¶ 33. Gralise prescriptions grew [redacted]% over the subsequent nine quarters, Appx666 at ¶ 9, 680 at ¶ 34 (compound quarterly growth rate). Wholesale sales of Gralise exploded from $[redacted] in its launching quarter to a total of $[redacted] in its first 22 months on the market, Appx666 at ¶ 9, 680 at ¶ 35. And Gralise outperformed other drugs that lacked the '340 patent's technology: Gralise doubled its market share of the gabapentinoid market from 2012 to 2013. Appx682 at ¶ 39, 666 at ¶ 9.

Depomed's Acuform technology, which includes the technology of the '340 Patent, has been included in ten different licensing agreements since 2002 that

have paid Depomed substantial upfront, milestone, and royalty payments. Appx1162-65, 1179-80, 1193-94, 1202-08, 1243-51, 1299-1300, 1340-41, 1363, 1373-78, 1405-08, 1480, 1491-97, 1516, 1527-34, 1562, 1581-83, 1590-93, 1607-10, 1664-70, 1697-98, 1701-02, 1709-10, 1716-20, 1755-56, 1761, 1768-69, 1775-76, 1778-80, 1811-15, 1825, 1833-34, 1838-44, 1873-74, 1898-04 (relevant sections of licensing agreements and SEC filings describing those agreements). In all, Depomed received over $[redacted] from licensing and collaborative agreements as a result of the '340 patent's technology. Appx687 at ¶ 46, 709-710 at ¶ 77. In 2014, Depomed sold its interests in future royalty and milestone payments under its licensing agreements to PDL BioPharma for $240 million. Appx1186, 1199-1200, 1210.

B. Institution of *Inter Partes* Review.

On April 17, 2014, while defending against a patent infringement suit brought by Depomed, Endo Pharmaceuticals, Inc. (Endo) petitioned for *inter partes* review of independent claim 1 and dependent claims 2-5 and 10-13 of the '340 patent. Endo asserted that those claims were obvious over various prior art references including, as relevant to this appeal, (1) a published patent application filed by Depomed in 1998 titled *Gastric-Retentive Oral Drug Dosage Forms for Controlled-Release of Highly Soluble Drugs*, listing John W. Shell as the inventor (Shell 1998); and (2) Shell 1998 in view of an article by Elpiniki Papadimitriou et

al., *Swelling Studies on Mixtures of Two Hydrophilic Excipients* (Papadimitriou). Appx89-90.

On September 29, 2014, the Board instituted *inter partes* review with respect to claims 1, 3-5, and 10-13 of the '340 patent. Appx206-207. The Board declined to review the patentability of claim 2. *Id.*

C. Prior Art At Issue.

1. Shell 1998 (an earlier Depomed patent publication) considered the problem of drugs that are administered in conventional tablets which initially overdose and then ultimately underdose the body over time due to poorly controlled release and poor gastric retention. Appx411. The solution that Shell 1998 proposed was to use a water-swellable polymer that would erode at a rate substantially lower than its swelling rate. Appx412. Shell 1998 included a long list of individual polymers that would potentially satisfy that requirement. Shell 1998 also noted that polymers that did not provide adequate controlled release on their own could be combined with other polymers to try to improve the outcome. Appx416. But while Shell 1998 included HPMC and PEO in its long list of polymers, it did not discuss, test, or recommend combining HPMC and PEO or suggest that either of these would not provide adequate controlled release on its own. Appx415. To the contrary, the data included in Shell 1998 indicated that HPMC and PEO each worked well on its own to provide controlled release. Shell

1998 thus offered no motivation to combine HPMC and PEO to improve either's controlled-release properties.

2. Papadimitriou studied combining PEO and HPMC for purposes unrelated to evaluating the resulting gastric-retentive or controlled-release quality of the combination. Papadimitriou's focus was on determining the "percolation threshold"—the point at which swelling properties are dominated by one or the other polymer in a combination matrix. Appx451. As a result, Papadimitriou is not a study of the effects of the combination as a whole, but rather a study of the complex interaction *between* polymers in combination. It also involved assays in a phosphate buffer with a pH of 7.4—much higher than the pH characteristic of the stomach (approximately 1.2)—and without any agitation that would mimic the harsh conditions of the stomach. In addition, because it did not include any drug substance with the combination, it could have no relevance as to what the controlled-release properties would be for a combined PEO-HPMC polymer. *Id.*

D. Board Decision.

The Board concluded that claims 1, 3-5, and 10-13 of the '340 patent were unpatentable as obvious. Appx2.[2] It first addressed whether the patent's claims

[2] There was no dispute during the Board proceedings as to who was a person of ordinary skill in the art at the time of the '340 patent; that person "would have a Bachelor's degree in chemistry or a similar discipline, and at least several years of work experience in the design and/or development of controlled release oral drug

were obvious in light of Shell 1998. Appx9. In its view, the "inferences and creative steps" that persons of ordinary skill in the art would apply to Shell 1998 would likely lead them to use HPMC and PEO in a combination matrix, rendering claim 1 obvious. *Id.* The Board concluded that Shell 1998 listed HPMC and PEO as "particularly preferred polymers" and that persons of ordinary skill in the art would thus have tried to combine them, despite the fact that Shell 1998 did not discuss, test, or recommend combining HPMC and PEO specifically or any of the "preferred polymers" with sufficient controlled release on their own. Appx15. The Board's reasoning was essentially that a person of skill in the art would have combined PEO and HPMC because Shell 1998 did not counsel against doing so: "The Shell 1998 Publication does not limit which polymers could be combined or suggest that certain polymers would not function properly in a combination matrix." *Id.* The Board also concluded that dependent claims 3-5 and 11-13 were unpatentable in light of Shell 1998. Appx17.

Turning to Shell 1998 and Papadimitriou together, the Board held that these two references rendered obvious claims 1, 3-5, and 10-13. Appx19. According to

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dosage forms." Appx9. There was also no dispute as to the meaning of the claim terms. The term "monolithic matrix" means "a matrix constructed as a single piece"; the term "to swell upon contact with gastric fluid to a size large enough to provide gastric retention" means "to increase in size upon contact with gastric fluid such that the tablet remains in the stomach"; and the term "gastric fluid" means "both the fluid in the stomach and simulated or artificial fluids recognized by those skilled in the art as a suitable model for the fluid of the human stomach." Appx7.

the Board, the mere fact that Papadimitriou discussed combining PEO and HPMC meant that, in combination with Shell 1998, a person of skill in the art would have intuited that PEO and HPMC would work together to produce a gastric-retentive, controlled-release tablet. To reach this conclusion, the Board held it was irrelevant that Papadimitriou's studies—conducted in conditions unrelated to the stomach and not including any drug—offered no guidance with respect to gastric retention or controlled release. Appx23; *see also* Appx28 (holding dependent claims invalid as obvious).

The Board then turned to the objective considerations of non-obviousness. Appx35. The Board found that Depomed had not shown that the success of Gralise was related to the '340 patent's invention, Appx36, even though Depomed had submitted a declaration from Dr. Harold Hopfenberg, an expert in controlled-release dosage forms, stating "that there is a direct nexus between the '340 patented technology and the Gralise® product." *Id.* (citation omitted). The Board gave little weight to Depomed's evidence of ten separate lucrative licenses incorporating the '340 patented technology. Appx37-38. It declined to address Depomed's evidence of a long-felt need for a gastric-retentive, controlled-release drug dosage form that could be administered once daily and would deliver highly soluble drugs slowly, evenly, and reproducibly. The Board believed that Depomed's evidence did not demonstrate "that others tried but failed to satisfy that

demand." Appx38-39 (citation omitted). The Board also rejected Depomed's evidence that undue experimentation was required to recognize the unexpected benefit that combining PEO with HPMC resulted in a gastric-retentive, controlled-release drug formulation. Appx39.

This appeal followed. After Endo withdrew as the appellee and named party in the appeal, the Director of the U.S. Patent and Trademark Office (PTO) exercised her right to intervene under 35 U.S.C. § 143.

SUMMARY OF THE ARGUMENT

The Board's conclusion that the '340 patent's claims are unpatentable as obvious was legally flawed. For starters, the patent itself documents the unexpected beneficial results of combining HPMC and PEO, and there was no dispute as to the fact that these results were unexpected. The Board's analysis failed entirely to account for the unexpected characteristics of the resulting polymer combination. Numerous precedents from this Court—many of which specifically deal with unexpected results in connection with combination drugs—hold that when the results are unexpected, an invention is not obvious. In addition, the Board applied a legally incorrect standard to assess whether there was a long-felt need for the invention claimed in the '340 patent. The Board grafted a totally novel and incorrect requirement onto the analysis, and then erroneously relied on its new requirement as a basis to reject Depomed's evidence of a long-felt need.

The Board's obviousness conclusion was further flawed because it relied on hindsight bias when reviewing the prior art. Polymer combinations were known to be unpredictable, and yet the Board held the '340 patent's claims obvious in light of two references that had no bearing—alone or together—on a PEO and HPMC combination in a gastric-retentive, controlled-release tablet. Shell 1998's suggestion to combine polymers did not apply to PEO and HPMC, because Shell 1998 found that those two polymers provided adequate controlled release on their own. And the study of PEO and HPMC in Papadimitriou—at neutral pH without any drug—is irrelevant to a gastric-retentive, controlled-release tablet.

The Board's errors continued through its assessment of the objective considerations of non-obviousness. Its legal missteps related to unexpected results and long-felt need undermine its factual findings on those points. And the Board was equally off-base in its assessment of the evidence related to the commercial success of several prescription drugs utilizing the '340 patent's technology and the patent's contribution to multimillion-dollar licensing agreements.

Finally, Depomed preserves an argument that the Board's decision should be vacated on the basis that the Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284, is unconstitutional. In that Act, Congress provided for the PTO to conduct *inter partes* review to evaluate the validity of a patent at the request of a third party. But the Supreme Court's public-rights jurisprudence makes clear that

Congress can only assign such a judicial power to an administrative agency if the right at issue is a public one. Supreme Court precedent holds that only an Article III court may decide a patent's validity after issuance. The *inter partes* review system thus violates Article III and the Seventh Amendment.

For these reasons, the Board's determination should be vacated or reversed.

STANDARD OF REVIEW

The ultimate determination of obviousness under 35 U.S.C. § 103(a) (2006) is a legal conclusion based on underlying findings of fact. *Rambus Inc. v. Rea*, 731 F.3d 1248, 1251-52 (2013). This Court reviews de novo the Board's "ultimate determination of obviousness and compliance with legal standards." *Pride Mobility Prods. Corp. v. Permobil, Inc.*, No. 2015-1585, 2016 WL 1321145, at *4 (Fed. Cir. Apr. 5, 2016). It reviews the Board's underlying factual findings for substantial evidence. *Id.; see also Randall Mfg. v. Rea*, 733 F.3d 1355, 1362 (Fed. Cir. 2013) ("On appeal, we review the Board's compliance with governing legal standards de novo and its underlying factual determinations for substantial evidence.").

In reviewing a conclusion of obviousness de novo, this Court takes care to avoid " 'the distortion caused by hindsight bias.' " *Zoltek Corp. v. United States*, 815 F.3d 1302, 1313 (Fed. Cir. 2016) (quoting *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 421 (2007)). "To imbue one of ordinary skill in the art with knowledge

of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher." *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1553 (Fed. Cir. 1983).

The constitutionality of *inter partes* review is reviewed de novo. *See SKF USA, Inc. v. U.S. Customs & Border Prot.*, 556 F.3d 1337, 1349 (Fed. Cir. 2009).

ARGUMENT

I. THE PTAB'S OBVIOUSNESS DETERMINATION WAS ERRONEOUS.

The Court should reverse the Board's determination that certain claims of the '340 patent are unpatentable as obvious. A patent is invalid for obviousness only if "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a) (2006).[3] Obviousness is not established "merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, 550 U.S. at 418. Rather, a patent is invalid for

[3] Although this provision was amended in 2011, *see* Pub. L. No. 112-29, § 6, 125 Stat. 284, 287-288 (2011), the amendment does not apply here because the application that led to the '340 patent was filed before March 16, 2013. *See* 125 Stat. at 293; *Q.I. Press Controls, B.V. v. Lee*, 752 F.3d 1371, 1377 n.3 (Fed. Cir. 2014).

obviousness only if "a skilled artisan would have had reason to combine the teaching of the prior art references to achieve the claimed invention, and [ ] the skilled artisan would have had a reasonable expectation of success from doing so." *PAR Pharm., Inc. v. TWI Pharm, Inc.*, 773 F.3d 1186, 1193 (Fed. Cir. 2014) (citation and internal quotation marks omitted).

Four aspects of the obviousness inquiry are directly relevant here. *First*, if a combination of two elements known in the prior art yields unexpected results, the unexpected nature of those results counsels against obviousness. *In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995) ("that which would have been surprising to a person of ordinary skill in a particular art would not have been obvious").

Second, long-felt but unmet need is a separate consideration from the failure of others, contrary to the Board's conflation of these distinct considerations. *See, e.g., In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1082 (Fed. Cir. 2012); *Procter & Gamble Co. v. Teva Pharm. USA, Inc.*, 566 F.3d 989, 998 (Fed. Cir. 2009). The Board's legal error in conflating these two separate inquiries prevented it from addressing the evidence of a long-felt need for a gastric-retentive, controlled-release formulation for many drugs. When an objective consideration like long-felt but unmet need is present, "it is error not to consider [it]." *In re Kao*, 639 F.3d 1057, 1067 (Fed. Cir. 2011).

Third, prior art cannot be examined with the distortion of hindsight bias. *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 36 (1966); *In re Cyclobenzaprine*, 676 F.3d 1063, 1079. The concern animating this principle is that, "knowing that the inventor succeeded in making the patented invention, a fact finder might develop a hunch that the claimed invention was obvious, and then construct a selective version of the facts that confirms that hunch." *Id.* To avoid hindsight bias, this Court looks to objective considerations, which "might serve to 'resist the temptation to read into the prior art the teachings of the invention in issue.' " *Id.* (quoting *Graham*, 383 U.S. at 36). This is especially true for inherently unpredictable technology, such as the combination of polymers at issue here.

And *finally*, the presence of objective considerations of non-obviousness like commercial success and licensing " 'can be the most probative evidence of non-obviousness in the record.' " *Crocs, Inc. v. Int'l Trade Comm'n*, 598 F.3d 1294, 1310 (Fed. Cir. 2010) (citation omitted).

Each of these principles undercuts the PTAB's determination here. The '340 patent is a textbook example of claims that do *not* involve combining familiar elements through a known method to yield predictable results.

A. The Board Committed Legal Error In Its Unexpected Results And Long-Felt Need Analysis.

1. The Board failed to analyze the unexpected properties of a combined PEO and HPMC matrix.

The '340 patent describes "unexpectedly beneficial performance" of the use of HPMC and PEO in combination. Appx55 at 3:33-40. The combination—to the surprise of Depomed's scientists—"avoid[ed] or substantially reduc[ed] the problems" associated with PEO or HPMC standing alone, specifically PEO's potential toxicology risks at high doses and HPMC's poor control of drug release. *Id.* at 3:11-30, 3:36-38. The combination also delivered unexpected benefits: The swelling behavior of PEO remained, but the erosion behavior of HPMC modulated the extent and progress of that swelling. *Id.* at 3:40-43. The swelling and erosion effects of the combined polymer also imbued the tablet with greater integrity, allowing it to disintegrate more slowly and evenly than those containing only PEO or only HPMC. *Id.* at 3:50-54; Appx58 at 9:46-48. That, in turn, led to more reproducible drug-release rates and transit times through the gastrointestinal tract. Appx55 at 3:50-59. As Dr. Bret Berner, one of the '340 patent's inventors noted, "the PEO and HPMC combination matrix provides unexpected beneficial performance." Appx755 at ¶ 24. The inventors "were able to obtain a surprisingly good balance of total swelling (for gastric retention), rate of swelling (to prevent esophageal blockage) and erosion (for reproducible disintegration of the dosage

form)." *Id.* The combination matrix also better controlled release of gabapentin than did either polymer standing alone. Appx58 at 9:3-49.

In the pharmaceutical context, this Court has often looked to whether unexpected results occurred from a combination—and upheld the patentability of combinations that provided such unexpected results. For example, in *Sanofi-Aventis Deutschland GmbH v. Glenmark Pharm. Inc., USA*, 748 F.3d 1354, 1361 (Fed. Cir. 2014), the Court rejected an obviousness challenge where persons of skill in the art would not have predicted that "longer lasting hypertension control" would result from the drug combination at issue given what was known about the individual components. *Id.* (noting credible testimony that persons of skill in the art "would not have predicted the longer-lasting hypertension control demonstrated by the double-ring structures of quinapril and trandolapril in combination with calcium antagonists, because of the widespread belief that double-ring inhibitors would not fit the pocket structure of the ACE").

Similarly, in *Pozen Inc. v. Par Pharmaceutical, Inc.*, 696 F.3d 1151, 1165 (Fed. Cir. 2012), the Court sustained a patent for a drug product when the combination was found to have longer-lasting efficacy than either component separately. As the Court explained, "the prior art would not have provided one of ordinary skill with motivation to combine sumatriptan and naproxen in order to benefit from longer lasting efficacy as compared to when either agent is taken

alone." *Id.* This type of unexpected result is particularly compelling in the pharmaceutical context because, "in the medical arts, 'potential solutions are less likely to be genuinely predictable.' " *Sanofi-Aventis*, 748 F.3d at 1360 (quoting *Eisai Co. v. Dr. Reddy's Labs., Ltd.*, 533 F.3d 1353, 1359 (Fed. Cir. 2008)).[4]

The unexpected benefits described in the '340 patent could not have been foreseen in light of the characteristics of each polymer individually. HPMC, for example, does not swell as much as PEO does, and was thought to erode faster. Appx55 at 3:23-27, 627-628 at ¶ 42, 755 at ¶ 22. It would have been reasonable, then, to suspect that combining HPMC and PEO would have reduced the gastric-retentive properties of the polymer and/or that it would have reduced control over the rate of drug release. Appx627-628 at ¶ 42, 755 at ¶ 23. What the inventors of the '340 patent discovered is that the mixture of PEO and HPMC actually provided excellent gastric retention. Moreover, it also—counterintuitively—provided better controlled release of gabapentin than did either polymer standing alone. Appx628 at ¶ 43.

[4] In contrast, when the elements of a combination are known in the prior art and the combination has not led to unexpected results, the Court has invalidated the patent. *E.g., Richardson-Vicks Inc. v. Upjohn Co.*, 122 F.3d 1476, 1477, 1484 (Fed. Cir. 1997) (patent claiming combination drug was obvious where it resulted in no unexpected properties for the combination of known products); *Merck & Co. v. Biocraft Labs., Inc.*, 874 F.2d 804, 809 (Fed. Cir. 1989) (patent was obvious where drug combination had no "unexpectedly good" properties compared with the separate components).

This Court has concluded that this sort of counterintuitive outcome is not an obvious one: Where "the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful," a determination of obviousness is premised only on improper hindsight bias. *In re Kubin*, 561 F.3d 1351, 1359 (Fed. Cir. 2009) (quoting *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988)). That is, an invention is obvious only if "there are a finite number of identified, predictable solutions" to a known problem. *KSR*, 550 U.S. at 421. Here, there certainly was no such "finite (and small in the context of the art) number of options easily traversed to show obviousness." *Ortho-McNeil Pharm., Inc. v. Mylan Labs, Inc.*, 520 F.3d 1358, 1364 (Fed. Cir. 2008). As in *Ortho-McNeil*, a person of ordinary skill in the art would "not even be likely to start" with either of the polymers that were ultimately combined in the '340 patent. *Id.* Nor would that person have "some reason to select (among several unpredictable alternatives) the exact route that produced" the patent's method. *Id.*

No prior art suggested that combining PEO and HPMC would enhance the beneficial properties—and mitigate the detrimental properties—of each. Even if each of the components of the patented polymer matrix had been identified in the prior art, none of that art hinted at the possibility of this beneficial synergy.

The Board ignored all of this, disregarding that Depomed invested time and money in testing more than a dozen polymer classes in dozens of formulations before arriving at the combination of PEO and HPMC. Appx39; *see* Appx751 at ¶ 15. Indeed, the Board did not even consider whether anything unexpected happened when PEO and HPMC were used in a combined matrix. That was legal error. Had the Board taken into account the evidence of unexpected results—as spelled out in the patent itself and the Berner and Hopfenberg declarations, Appx55 at 3:32-4:21; Appx627-628 at ¶¶ 41-45; Appx755 at ¶ 24—the Board would have come to the same conclusion as this Court did in *Sanofi-Aventis*, *Pozen*, and *Ortho-McNeil*: the patent's invention is not obvious.

2. The Board conflated the separate considerations of long-felt need and failure of others.

The Board's analysis contains a second legal error: It held that to demonstrate a long-felt need, the patentee must offer "evidence that others tried and failed" to meet a demand later solved by the patent at issue. Appx39. That is not—and has never been—the test for evaluating whether a long-felt but unmet need was overcome by a patented invention. The Board cited *In re Cyclobenzaprine* for the proposition that a patent owner "*must show* that any evidence of long-felt need 'demonstrates both that a demand existed for the patented invention, and that others tried but failed to satisfy that demand.' " *Id.* (emphasis added) (quoting *In re Cyclobenzaprine*, 676 F.3d 1063, 1082).

But *In re Cyclobenzaprine* holds no such thing. For starters, the actual sentence the Board was quoting states that "[e]vidence is particularly probative of obviousness when it demonstrates both that a demand existed for the patented invention, and that others tried but failed to satisfy that demand." 676 F.3d at 1082. Nothing in that sentence, or anything else in the decision, indicates that demonstrating a long-felt need *requires* a showing that others have failed. To the contrary, the patentee in that case asserted—and the Court agreed—that *two* objective considerations "strongly support[ed] a conclusion of nonobviousness": (1) "the failure of others," and (2) "a longfelt need for an extended-release formulation." *Id.* at 1080. As the Court explained, it "address[ed] *each* of these considerations." *Id.* (emphasis added). In fact, it did so by laying them out in separate sections of the decision. *Id.* at 1081-82 (addressing the failure of others in section 3(a) and long-felt need in section 3(b)).

The Court determined that the long-felt-need consideration supported a finding of non-obviousness because there was proof "that a longfelt need existed for a therapeutically effective, extended-release cyclobenzaprine formulation." *Id.* at 1083. The proof was that an immediate-release formulation had existed for decades, "but that formulation's regimen of multiple daily doses led to poor patient compliance." *Id.* The Court went on to say that "[a]s discussed above, moreover, others tried but failed to develop an extended-release version," and that a physician

testified about the importance of patient compliance with a medical regimen and the more convenient dosing offered by the extended-release formulation. *Id.*

Other decisions from this Court similarly confirm that proof of a long-felt need does not require proof of the failure of others. For example, in *Procter & Gamble*, 566 F.3d 989 (Fed. Cir. 2009), the Court affirmed the finding that there was a long-felt but unmet need for a particular drug based on the fact that at the relevant time the disease it treated (osteoporosis) "was recognized as a serious disease and existing treatments were inadequate." *Id.* at 998; *see also Ferring B.V. v. Watson Labs., Inc.-Fl.*, 764 F.3d 1401, 1407 (Fed. Cir. 2014) (holding that "supporting evidence demonstrated that there was a long-felt and unmet need for a treatment for menorrhagia that avoided adverse events"); *Geo. M. Martin Co. v. All. Mach. Sys. Int'l LLC*, 618 F.3d 1294, 1304-05 (Fed. Cir. 2010) (separately analyzing evidence of long-felt need and evidence of failure of others).

Had the Board examined Depomed's evidence of a long-felt need rather than rejected it solely on the basis that it did not show the failure of others, the Board would have concluded that Depomed did present proof of a long-felt but unmet need. Before the '340 patent was invented, once-daily, gastric-retentive, controlled-release dosage forms were desperately needed to deliver certain highly soluble drugs slowly, evenly, and reproducibly. Appx758-759 at ¶¶ 31-33, 648-649 at ¶¶ 98-99. The case of metformin exemplifies this long-felt need and

precisely how the '340 patent met that need. Prior to invention of the '340 patent's claims, the available, immediate-release dosage forms had to be taken two to three times a day and often resulted in side effects like nausea and diarrhea. Appx758 at ¶ 31. Those side effects led to poor patient compliance, discontinuation of therapy, and/or inadequate dosing for complete therapeutic effect. *Id.* Glumetza, a tablet for diabetics that incorporates the '340 patent's technology, fulfilled that long-felt need by allowing patients to take the drug only once daily. *Id.* The drug's gastric-retentive and controlled-release properties reduced nausea and diarrhea and improved compliance at the highest effective dose. *Id.*

The '340 patent served patients suffering from postherpetic nerve pain equally well. As early as 1993, scientists recognized that gabapentin was not well absorbed into the colon. Appx758-759 at ¶ 32. As a result, patients had to take immediate-release gabapentin three times daily and often suffered from resulting dizziness and sleepiness. *Id.* Patient compliance suffered. *Id.* Gralise, which incorporates the '340 patent's technology, allowed for once-daily, gastric-retentive, controlled-release administration of a drug, increasing patient compliance and reducing dizziness and sleepiness. *Id.*

The Board's decision to discount all of this evidence of long-felt but unmet need because the evidence did not address the failure of others was legal error. The presence of such an objective consideration of non-obviousness—just like the

unexpected results described above—is highly probative evidence of non-obviousness. *Procter & Gamble*, 566 F.3d at 998 (explaining that "[w]hen present, such factors 'may often be the most probative and cogent evidence [of non-obviousness] in the record.' " (citation omitted; second alteration in original).

B. The Board's Review Of The Prior Art Was Improperly Based On Hindsight.

The Board's analysis of the prior art was similarly erroneous, because it analyzed the prior art through the distorted lens of hindsight bias. No prior art reference, alone or in combination, taught that one could combine PEO and HPMC to create a matrix at a weight ratio that would "cause[ ] said matrix to swell upon contact with gastric fluid to a size large enough to provide gastric retention," as disclosed in claim 1. Appx59 at 11:66-67. Nor did any of the prior art render it obvious that combining PEO and HPMC would result in a gastric-retentive, controlled-release dosage form that would benefit patients by reducing side effects and allowing for less frequent dosing.

1. Shell 1998 does not render obvious any claim of the '340 patent.

Shell 1998 provides a long list of potentially useful polymers. No fewer than seven of those polymers are referred to as "preferred" polymers—PEO, HPMC, hydroxyethyl cellulose, xanthan gum, and three different grades of crosslinked polyacrylic acid. Appx415. Shell 1998 employs the polymers in 28

formulations, none of which is a combination of PEO and HPMC. In fact, the vast majority of the formulations—24 of the 28—disclosed in Shell 1998 are *individual* swellable polymers, not combinations of polymers. *See* Appx419-425.

To the extent that Shell 1998 discloses polymer combinations, it does so as a possible mechanism for overcoming certain polymers' deficiency in controlled release. Appx632-633 at ¶ 56. Thus, all of the polymer combinations in Shell 1998 involve either xanthan gum or hydroxyethyl cellulose, neither of which exhibits adequate early control of drug release on its own. *Id.*; *see also* Appx416 at 6:32-36, 422 at 12:13-16, 423 at 13:22-29, 424 at 14:1-5. In contrast, Shell 1998 does not disclose any condition under which either PEO or HPMC failed to achieve sufficient early control of drug release. It thus does not suggest that either PEO or HPMC should be combined with any other polymer.

Shell 1998 also confirms that polymer combinations have varied and unpredictable effects on the characteristics of the component polymers. For example, combining HPMC with hydroxyethyl cellulose did not improve hydroxyethyl cellulose's poor gastric retention. But combining PEO with hydroxyethyl cellulose did. Appx635-636 at ¶ 63; *see also* Appx434 at Figure 6. This lack of predictability as to polymer combination goes directly to the root of the problem the '340 patent was trying to solve: Dr. Hopfenberg, an expert on controlled-release dosage forms, testified that "[t]hese structural variations can

significantly affect the properties that are critical for a gastric-retentive controlled release form, including swelling, drug release, mechanical integrity, and the tendency to undergo long term degradation of the matrix of the dosage form subsequent to the designed release." Appx634 at ¶ 59. Because of the unpredictability of polymer combinations, a person of ordinary skill in the art would have had no motivation to combine two polymers that already satisfied the criteria for inclusion in Shell 1998's list of polymers that achieved the desired controlled release. Appx636 at ¶ 64. Nothing in Shell 1998 suggested that a combination of PEO and HPMC would create a more desirable dosage form, or even an acceptable dosage form.

Thus, Shell 1998 did not render the combination of HPMC and PEO "obvious to try." An invention is obvious to try only where "the possible options skilled artisans would have encountered were 'finite,' 'small,' or 'easily traversed,' and . . . skilled artisans would have had a reason to select the route that produced the claimed invention." *In re Cyclobenzaprine*, 676 F.3d at 1072 (quoting *Ortho-McNeil*, 520 F.3d at 1364).

The Board's reasoning basically concludes that Shell 1998 made it "obvious to try" any combination of the many polymers described in that publication. That is plainly wrong. Even if the calculation is limited to the seven polymers referred to in Shell 1998 as "preferred," there would be forty-two distinct two-preferred-

polymer combinations. Particularly given that Shell also disclosed the need to assess—for each polymer combination—different polymer proportions, different drug-to-polymer ratios, different drug doses, and different particle sizes, *see* Appx416 at 6:10-14 & 6:19-21, 637 at ¶ 67, 1060-61 at 85:22-86:2, 1059 at 78:17-23, 1064 at 99:16-24, Shell 1998 is a far cry from a roadmap to developing the '340 patent; it offers nothing more than the possibility of "throw[ing] metaphorical darts at a board" to divine a solution to the problem later solved by the '340 patent. *See In re Kubin*, 561 F.3d at 1359.

2. Shell 1998 and Papadimitriou together do not render obvious any claim of the '340 patent.

This Court has recognized time and time again that "even when all claim limitations are found in prior art references, the factfinder must not only determine what the prior art teaches, but whether the prior art teaches away from the claimed invention and whether there is a motivation to combine teachings from separate references." *Star Sci., Inc. v. R.J. Reynolds Tobacco Co.*, 655 F.3d 1364, 1374-75 (Fed. Cir. 2011). Not only must there be a motivation for a person of ordinary skill in the art to combine the teachings from disparate references; he must also have "a reasonable expectation of success from doing so." *In re Cyclobenzaprine*, 676 F.3d at 1069 (citation omitted).

Here, the Board did what this Court has consistently held that it must not do: it "allow[ed] hindsight reconstruction of references to reach the claimed invention

without any explanation as to how or why the references would be combined to produce the claimed invention." *Kinetic Concepts, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1342, 1368 (Fed. Cir. 2012) (quoting *Innogenetics, N.V. v. Abbott Labs.*, 512 F.3d 1363, 1374 n.3 (Fed. Cir. 2008)). Viewing the prior art with hindsight bias is error. The Board compounded its error by failing to consider the prior art holistically. "When prior art contains apparently conflicting references, the Board must weigh each reference for its power to suggest solutions to an artisan of ordinary skill." *In re Young*, 927 F.2d 588, 591 (Fed. Cir. 1991). In other words, the Board is bound to "consider the degree to which one reference might accurately discredit another." *Id.*

Here, the Board ignored critical aspects of the prior art that show why no person having ordinary skill in the art would have combined Shell 1998 with Papadimitriou to obtain the '340 patent's invention. Papadimitriou's study of a PEO and HPMC combination gave no hint at what the effect of this combination would be in terms of gastric retention—a critical feature of the '340 patent. The study did not use a pH that mimicked the stomach; it used a neutral pH. Appx451. And it involved no agitation. *Id.* As a result, it neither explicitly nor implicitly had any application to the harsh conditions of the stomach, in which many dosage forms simply fall apart rather than being retained.

Moreover, the tablets in Papadimitriou contained *no drug at all*, so it would have been impossible for Papadimitriou to give any suggestion about what sort of controlled release would result from a PEO and HPMC combination. *Id.* To the extent Papadimitriou speculated that combining PEO and HPMC could "have implications for release processes of drugs" it assumed that controlled release was merely a function "of the degree of swelling that occurs." *Id.* It did not address at all the potential toxicity of PEO or the too-quick erosion of HPMC. Most critically, nothing in Papadimitriou can be read to suggest the critical *synergistic benefit* revealed by the '340 patent—that PEO and HPMC together provided better controlled release of gabapentin than either polymer alone.

There is no way—except through hindsight bias—that the combination of Shell 1998 and Papadimitriou would point a person of ordinary skill in the art to any solution with regard to the particular problem solved by the '340 patent. Studying any two of Shell 1998's particularly preferred polymers—without evaluating the effect of the combination on gastric retention—gets one no closer to the '340 patent's solution than did Shell 1998 standing alone.

C. Secondary Considerations Reinforce That The '340 Patent's Claims Are Not Obvious.

Objective indicia of non-obviousness are critical to combatting improper hindsight bias. They can establish that " 'an invention appearing to have been obvious in light of the prior art was not.' " *Rambus*, 731 F.3d at 1256 (quoting

Stratoflex, Inc. v. Aeroquip Corp., 713 F.2d 1530, 1538 (Fed. Cir. 1983)). The Board did not properly apply this check against hindsight bias.

As described above, because of legal error, the Board ignored the evidence of the unexpected results. *Supra*, 22-26. As also described above, because of legal error, the Board failed to acknowledge the long-felt need for a gastric-retentive, controlled-release dosage formulation, particularly for drugs like gabapentin and metformin. *Supra*, 26-30. The Board's assessment of other objective indicia is just as unsupportable.

1. The '340 patent required undue experimentation.

Where "extensive experimentation . . . was required to arrive at [the] particular compound" claimed in the patent, that is strong evidence that it would not have been obvious to a person of ordinary skill in the art to arrive at the patent's claims. *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1379 (Fed. Cir. 2006). It required one and a half years of extensive experimentation by the '340 patent's inventors to arrive at just the right blend of PEO and HPMC. Appx751-755 at ¶¶ 15-24. The inventors, who were seeking to develop a once-daily metformin dosage form, Appx750 at ¶ 12, toiled for well over a year, testing dozens of formulations covering many polymer classes. Appx751-752 at ¶ 15. For each potentially viable formulation, the inventors conducted drug release studies, disintegration tests, swelling tests, mechanical integrity tests, stability of drug tests,

and stability of tablet tests. Appx752 at ¶ 16. These tests required Depomed to create its own swelling and erosion assays. Appx752-753 at ¶¶ 17-18. The next step of testing, for those formulations that passed this extensive review, assessed gastric retention in dogs. Appx752 at ¶ 16. If that test, too, was successful, the inventors performed pharmacokinetic studies in the dogs, taking days to weeks. *Id.*

The Board gave "little weight" to this extensive experimentation based on its view that Depomed's scientists used PEO early in their efforts and suggested using HPMC a month later. Appx39. That is wrong for two reasons. First, the rigorous testing to find the right combination was not merely "work to satisfy particular commercial requirements." Appx40. As Shell 1998 itself observed, assessing any polymer combination requires testing different polymer proportions, different drug-to-polymer ratios, different drug doses, and different particle sizes. Appx416 at 6:10-14 & 6:19-21, 637 at ¶ 67, 1059 at 78:17-23, 1060-61 at 85:22-86:2, 1064 at 99:16-24. And second, the fact that the scientists also studied dozens of other formulations during this year and a half, Appx751-752 at ¶ 15, reinforces that the discovery of the exact formulation involving the precise viscosity, molecule weight, and weight ratio described in the '340 patent did not occur the moment that someone first suggested testing PEO and HPMC. Rather, it took significant experimentation to achieve the results of the '340 patented invention.

2. The ’340 patent was a commercial success.

Commercial success resulting from a claimed invention weighs in favor of a patent’s non-obviousness. *J.T. Eaton & Co. v. Atl. Paste & Glue Co.*, 106 F.3d 1563, 1571 (Fed. Cir. 1997). “When a patentee can demonstrate commercial success, usually shown by significant sales in a relevant market, and that the successful product is the invention disclosed and claimed in the patent, it is presumed that the commercial success is due to the patented invention.” *Id.* A nexus is inferred when the patentee shows “ ‘that there is commercial success, and that the thing (product or method) that is commercially successful is the invention disclosed and claimed in the patent.’ ” *Iron Grip Barbell Co. v. USA Sports, Inc.*, 392 F.3d 1317, 1324 (Fed. Cir. 2004) (quoting *Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387, 1392 (Fed. Cir. 1988)). This test is satisfied by Depomed’s evidence of Gralise’s success and its profits stemming directly from its incorporation of the ’340 patent’s Acuform technology.

The Board erred by failing to consider Depomed’s extensive evidence of the nexus between Gralise’s commercial success and the ’340 patent, which further supports the nonobviousness of the patent. *See* Appx36. Dr. Hopfenberg, for one thing, opined that there is a “direct nexus between the ’340 patent’s technology and the Gralise® product.” Appx648 at ¶¶ 96-97. That opinion tracks this Court’s description of the standard to show commercial success. *See Ormco Corp. v. Align*

Tech., Inc., 463 F.3d 1299, 1311-12 (Fed. Cir. 2006) ("Evidence of commercial success . . . is only significant if there is a nexus between the claimed invention and the commercial success."); *Richdel, Inc. v. Sunspool Corp.*, 714 F.2d 1573, 1580 (Fed. Cir. 1983) (holding claimed invention obvious where patent holder "failed to show that such commercial success . . . was due to anything disclosed in the patent in suit which was not readily available in the prior art"). The Board also disregarded Dr. Hopfenberg's statement that Gralise embodies each and every limitation in the claims of the '340 patent—apparently on the basis that Depomed cited to his declaration in its response rather than also cutting and pasting a 9-page claim chart into its response. Appx36. Dr. Hopfenberg's declaration stated:

> It is my opinion that the 300 mg and 600 mg Gralise® Tablets fall within the scope of and, therefore, embody the relevant claims of the '340 Patent, supporting a conclusion that the commercial success of the Gralise® tablets is due to their patented features. As set forth in my analysis presented in Appendix A (Exh. 2011), the composition and properties of 300 mg and the 600 mg Gralise® Tablets are within the scope of the properly construed relevant claims of the '340 Patent.

Appx648. And Appendix A to his declaration contains the claim chart. Appx651-659. Ignoring this evidence was particularly improper because it was not controverted by any other evidence in the record.

Similarly, Endo offered no evidence that Gralise's success was due to anything other than its patented features—including that it provided gastric retention and controlled release of gabapentin, allowing once-a-day administration

and reducing side effects as compared to other drugs for postherpetic neuralgia. Appx668 at ¶ 12, 697-702 at ¶¶ 60-67. And the record was replete with evidence that Gralise had been a commercial success. It generated more than [redacted] prescriptions in its first 27 months on the market. Appx666 at ¶ 9, 678-679 at ¶ 32. It generated $[redacted] in wholesale sales in its first 22 months on the market. Appx666 at ¶ 9, 680 at ¶ 35. Dr. Sean Nicholson, a Cornell University professor whose research focuses on the economics of healthcare, estimates that Gralise will generate $[redacted] more in profits in its first thirteen years than would a similar investment. Appx692 at ¶ 53. And Gralise even attracts patients from the much-cheaper generic immediate-release gabapentin because the gastric-retentive, controlled-release formulation allows for once-daily administration and has fewer side effects. Appx694 at ¶ 55, 697-703 at ¶¶ 60-67. It is hard to imagine clearer evidence of a direct nexus than the fact that patients are willing to spend *more* to purchase a tablet whose distinguishing feature is incorporation of the '340 patent's technology.

3. Depomed has licensed the '340 patent to the tune of [redacted]

Yet another indicator of non-obviousness is present: Depomed has licensed the '340 patent's technology repeatedly. And licensing activities "provide 'probative and cogent evidence' of non-obviousness of the claims at issue." *Institut Pasteur & Universite Pierre et Marie Curie v. Focarino*, 738 F.3d 1337,

1347 (Fed. Cir. 2013) (quoting *Stratoflex*, 713 F. 2d at 1538). Depomed has entered into ten different license agreements since 2002 for the '340 patent's technology. Appx1162-65, 1179-80, 1193-94, 1202-08, 1243-51, 1299-1300, 1340-41, 1363, 1373-78, 1405-08, 1480, 1491-97, 1516, 1527-34, 1562, 1581-83, 1590-93, 1607-10, 1664-70, 1697-98, 1701-02, 1709-10, 1716-20, 1755-56, 1761, 1768-69, 1775-76, 1778-80, 1811-15, 1825, 1833-34, 1838-44, 1873-74, 1898-04 (relevant sections of licensing agreements and SEC filings describing those agreements). Those licenses have resulted in significant upfront, milestone, and royalty payments for Depomed. As of December 2014, Depomed had generated over $[redacted] in licensing and collaborative agreements related to the '340 patent's technology. Appx687 at ¶ 46, 709-710 at ¶ 77. In 2014, Depomed sold its interests in future royalty and milestone payments to PDL BioPharma for $240.5 million. Appx1186, 1199-1200, 1210.

The Board disregarded these licenses on the basis that Depomed did not "establish whether the licensing program was successful because of the merits of the claimed invention or for other economic reasons, such as to avoid litigation or because of prior business relationships." Appx38. This Court has already rejected that crabbed view of licensing evidence. A patent owner need only demonstrate that its licenses were "reasonably commensurate with the scope of the claims," *Rambus*, 731 F.3d at 1257 (citation omitted), and Depomed did precisely that. It

clearly observed that the licenses were for products that used the Acuform technology, including the technology claimed in the '340 patent. Appx286-288.

A patent owner is under no obligation to affirmatively assert that no other "economic reasons" may have played a part. In *Rambus*, this Court rejected the Board's reasoning that licensing evidence could not support non-obviousness because "competitors have many reasons for taking licenses which are not necessarily related to unobviousness"—a close cousin of the language used by the Board here. 731 F.3d at 1257 (citation omitted). The Board's naked claim of a lack of nexus in *Rambus*, without supporting evidence that the licenses were purchased for reasons unrelated to the patent's claims or that they "stemmed from other licensed Rambus patents" required reversal on substantial evidence review. *Id.*

So too here. As in *Rambus*, the Board dismissed Depomed's asserted nexus to the '340 patent's claims because it could imagine other, hypothetical reasons why nine different companies would be willing to enter into a combined total of ten different licensing agreements, compensating Depomed to the tune of $[redacted] for the right to use Acuform technology. But imagining does not substantial evidence make. Nor does imagining shift the burden of proof from the challenger to the patent owner to prove nonobviousness. *See Magnivision, Inc. v.*

Bonneau Co., 115 F.3d 956, 962 (Fed. Cir. 1997) (holding that applying the wrong burden of proof is grounds for reversal or vacatur).

* * *

The Board erroneously failed to give appropriate weight to these objective indicia of non-obviousness, which make clear that the '340 patent's technology was not obvious in light of the prior art.

II. THE *INTER PARTES* REVIEW SCHEME VIOLATES ARTICLE III AND THE SEVENTH AMENDMENT.

Article III of the U.S. Constitution provides that "[t]he judicial Power of the United States, shall be vested in one supreme Court, and in such inferior Courts as the Congress may from time to time ordain and establish." U.S. Const. art. III, § 1.[5] That assignment of the judicial power is exclusive: "the 'judicial Power of

[5] Depomed acknowledges this Court's recent holding that the Board's *inter partes* review process does not violate Article III or the Seventh Amendment. *MCM Portfolio LLC v. Hewlett-Packard Co.*, 812 F.3d 1284 (Fed. Cir. 2015). In light of pending and anticipated petitions for certiorari addressing this question, Depomed preserves an argument that *inter partes* review is unconstitutional. *See Cooper v. Lee*, No. 15-955 (docketed Jan. 28, 2016); *MCM Portfolio LLC v. Hewlett-Packard Co.*, No. 15A872 (filed Feb. 18, 2016) (application to extend the time to file a petition for a writ of certiorari granted until April 29, 2016). Although Depomed did not raise these arguments before the Board, it was not required to do so because "[r]esolution of [the] . . . issue does not require the development of a factual record, the application of agency expertise, or the exercise of administrative discretion." *Beard v. Gen. Servs. Admin.*, 801 F.2d 1318, 1321 (Fed. Cir. 1986) (citation omitted). What is more, raising these claims would have been futile; the Board already had rejected these challenges in *Cooper* and *MCM Portfolio*. *See id.* ("since the Board's view of its authority in reviewing

the United States' . . . can no more be shared" with another branch than "the Chief Executive, for example, can share with the Judiciary the veto power, or the Congress share with the Judiciary the power to override a Presidential veto." *Stern v. Marshall*, 131 S. Ct. 2594, 2608 (2011) (quoting *United States v. Nixon*, 418 U.S. 683, 704 (1974)). In general, then, Congress may not "withdraw from judicial cognizance any matter which, from its nature, is the subject of a suit at the common law, or in equity or admiralty." *Murray's Lessee v. Hoboken Land & Improvement Co.*, 59 U.S. (18 How.) 272, 284 (1856). To the extent an Article I tribunal, including the Board, attempts to exercise that judicial power, "the proceeding was void; for the officers who performed these acts could exercise no part of that judicial power." *Id.* at 275.

The Supreme Court has made a limited exception for "public rights," which Congress may constitutionally assign to legislative or Article I courts. *N. Pipeline Constr. Co. v. Marathon Pipe Line Co.*, 458 U.S. 50 (1982) (plurality opinion). Three categories of rights fit within this exception: *first*, those rights arising between the government and private persons "subject to its authority in connection with the performance of the constitutional functions of the executive or legislative

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penalties was fully settled, '[r]aising this claim to the [Board] . . . would have been an exercise in futility, and presents an exception to the exhaustion doctrine.") (brackets and ellipses in original) (quoting *Hatcher v. Dep't of the Air Force*, 705 F.2d 1309, 1312 n.2 (11th Cir. 1983)).

departments," *Crowell v. Benson*, 285 U.S. 22, 50 (1932); *second*, those rights deriving "from a federal regulatory scheme," *Stern*, 131 S. Ct. at 2613; and *third*, those rights in which "resolution of the claim by an expert government agency is deemed essential to a limited regulatory objective within the agency's authority," *id.*

These limited exceptions do not encompass post-issuance determinations of patent validity. In *McCormick Harvesting Mach. Co. v. Aultman*, 169 U.S. 606, 609 (1898), the Supreme Court definitively resolved any question on this issue. It stated that "[t]he only authority competent to set a patent aside, or to annul it, or to correct it for any reason whatever, is vested in the courts of the United States, and not in the department which issued the patent." That makes sense. After all, once a patent has issued, it no longer involves a "public right." The very issuance of the patent means that the invention "has been taken from the people, from the public, and made the private property of the patentee." *United States v. Am. Bell. Tel. Co.*, 128 U.S. 315, 370 (1888) (discussing patents for land). Indeed, the Court reaffirmed the vitality of these 19th century cases just last term, when it approvingly quoted *Jones v. Campbell*, 104 U.S. 356, 358 (1882), for the proposition that " '[a patent] confers upon the patentee an exclusive property in the patented invention which cannot be appropriated or used by the government itself, without just compensation, any more than it can appropriate or use without

compensation land which has been patented to a private purchaser.' " *Horne v. Dep't of Agric.*, 135 S. Ct. 2419, 2427 (2015) (brackets in original).

The Court's 2011 decision in *Stern v. Marshall* supports the conclusion that only Article III courts can declare an issued patent invalid. The Bankruptcy Act of 1984, Pub. L. No. 98-353, 98 Stat. 333, allowed a bankruptcy court to enter final judgment on state law counterclaims in core bankruptcy actions. Because such state law counterclaims were "independent of the federal bankruptcy law" and "not necessarily resolvable by a ruling on the creditor's proof of claim in bankruptcy," the Court concluded that resolving them was an exercise of the judicial power. 131 S. Ct. at 2611.

Adjudicating those counterclaims could not fall within the public rights exception, because they did not depend on the "will of [C]ongress," and were not limited, currently or historically, to pursuit by the executive or the legislative branches. *Murray's Lessee*, 59 U.S. (18 How.) at 284; *N. Pipeline Constr.*, 458 U.S. at 68. The claimed right to relief did not flow from a statutory scheme. *See Thomas v. Union Carbide Agric. Prods. Co.*, 473 U.S. 568, 584-85 (1985). And the authority to decide the state law counterclaim was not limited to a "particularized area of the law." *See N. Pipeline Constr.*, 458 U.S. at 85. Therefore, the Court held, the bankruptcy court lacked the constitutional authority to adjudicate the state law counterclaims. *Stern*, 131 S. Ct. at 2620. The Court left

to another day whether "a particular agency can adjudicate legal issues under a substantive regulatory scheme." *Id.* at 2615.

Supreme Court precedent concludes that patent validity must be determined by an Article III court. And nothing in the Court's subsequent public rights jurisprudence has transformed the private rights flowing from issued patents into public ones. The AIA's delegation of the judicial power to the PTO to adjudicate those private rights thus violates Article III.

For related reasons, *inter partes* review deprived Depomed of its right to trial by jury. The Seventh Amendment provides that "[i]n Suits at common law, where the value in controversy shall exceed twenty dollars, the right of trial by jury shall be preserved." U.S. Const. amend. VII. And the Supreme Court has been clear that Congress "lacks the power to strip parties contesting matters of private right of their constitutional right to a trial by jury." *Granfinanciera, S.A. v. Nordberg*, 492 U.S. 33, 52-53 (1989). That is so because "to hold otherwise would be to permit Congress to eviscerate the Seventh Amendment's guarantee by assigning to administrative agencies or courts of equity all causes of action not grounded in state law, whether they originate in a newly fashioned regulatory scheme or possess a long line of common-law forebears." *Id.* at 52. Because an issued patent's validity is a matter of private right, the AIA's attempt to divest

patent owners of their right to a jury trial by purporting to empower the PTAB to adjudicate patent validity violates the Seventh Amendment.

CONCLUSION

For the foregoing reasons, the Board's judgment should be vacated or reversed.

Respectfully submitted,

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Dated: April 29, 2016

ADDENDUM

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Paper 68
Entered: September 16, 2015

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ENDO PHARMACEUTICALS, INC.,
Petitioner,

v.

DEPOMED, INC.,
Patent Owner.

Case IPR2014-00652
Patent 6,723,340 B2

Before GRACE KARAFFA OBERMANN, GEORGIANNA W. BRADEN, and TINA E. HULSE, *Administrative Patent Judges*.

BRADEN, *Administrative Patent Judge*.

FINAL WRITTEN DECISION
35 U.S.C. § 318 and 37 C.F.R. § 42.73

I. INTRODUCTION

We have jurisdiction to hear this *inter partes* review under 35 U.S.C. § 6(c). This Final Written Decision is issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. For the reasons that follow, we determine that Petitioner has shown by a preponderance of the evidence that claims 1, 3–5, and 10–13 of U.S. Patent No. 6,723,340 B2 (Ex. 1001, "the '340 patent") are unpatentable. We also address the parties' Motions to Exclude.

A. Procedural History

Endo Pharmaceuticals, Inc. ("Petitioner") filed a Corrected Petition (Paper 5, "Pet.") to institute an *inter partes* review of claims 1–5 and 10–13 of the '340 patent pursuant to 35 U.S.C. § 311. Depomed, Inc. ("Patent Owner") filed a Preliminary Response (Paper 11, "Prelim. Resp."). Pursuant to 35 U.S.C. § 314(a), we instituted an *inter partes* review of claims 1, 3–5, and 10–13 on the following grounds alleged in the Petition.

Reference(s)	Basis	Claims challenged
Shell 1998 Publication[1]	§ 103	1, 3–5, and 10–13
Shell 1998 Publication and Papadimitriou[2]	§ 103	1, 3–5, and 10–13
Edgren[3] and Papadimitriou	§ 103	1, 3–5, and 10–13

Paper 12 ("Dec. to Inst."), 29.

[1] WO 1998/55107, PCT/US98/11302, issued Dec. 10, 1998 (Ex. 1003, "Shell 1998 Publication").
[2] Papadimitriou E., et. al., "*Swelling studies on mixtures of two hydrophilic excipients*," S.T.P. Pharma. Sciences Vol. 3, issue 3, pages 232–236 (Jun. 1993) (Ex. 1007, "Papadimitriou").
[3] U.S. Patent No. 4,871,548, issued Oct. 3, 1989 (Ex. 1006, "Edgren").

After institution of trial, Patent Owner filed a Patent Owner Response (Paper 25, "PO Resp."),[4] to which Petitioner filed a Reply (Paper 41, "Reply").

In addition, Petitioner filed a Motion to Exclude. Paper 51 ("Pet. Mot. Exclude"). Patent Owner filed an Opposition to Petitioner's Motion to Exclude (Paper 56, "PO Exclude Opp."), and Petitioner filed a Reply (Paper 58, "Pet. Exclude Reply"). Patent Owner also filed a Motion to Exclude. Paper 53 ("PO Mot. Exclude"). Petitioner filed an Opposition to Patent Owner's Motion to Exclude (Paper 54, "Pet. Exclude Opp."), and Patent Owner filed a Reply (Paper 59, "PO Exclude Reply"). Patent Owner also filed observations on the cross-examination of Petitioner's declarant (Paper 52), to which Petitioner filed a response (Paper 55).

An oral argument was held on June 15, 2015. A transcript ("Tr.") of the oral argument is included in the record.[5] Paper 67.

B. Related Proceedings

Petitioner informs us that the '340 patent is involved in the following co-pending federal district court cases: *Depomed, Inc. v. Actavis Elizabeth LLC*, 3:12-cv-01358-JAP-TJB (D.N.J.); *Depomed, Inc. v. Endo Pharms.*

[4] Patent Owner filed a confidential Patent Owner Response (Paper 24) and a public Patent Owner Response (Paper 25) to which Petitioner filed a confidential Reply (Paper 40) and a public Reply (Paper 41). All citations in this Final Written Decision are to the public Patent Owner Response (Paper 25) and public Petitioner Reply (Paper 41).

[5] The parties filed joint Objections to Demonstrative Exhibits. Paper 64. In this Final Written Decision, we rely directly on the arguments presented properly in the parties' briefs and the evidence of record. The demonstrative exhibits were only considered to the extent they are consistent with those arguments and evidence, therefore, the objections are overruled.

Inc., 3:13-cv-02467-JAP-TJB (D.N.J.)*; Depomed, Inc. v. Purdue Pharma L.P.*, 3:13-00571 JAP-TJB (D.N.J.)*; Depomed, Inc. v. Zydus Pharm. (USA), Inc*., 3:12-cv-02813-JAP-TJB (D.N.J.)*; Depomed, Inc. v. Sun Pharma Global FZE*, 3:11-CV-03553 (D.N.J.)*; Depomed, Inc. v. Impax Labs., Inc.*, 3:12-CV-02154 (D.N.J.)*; Depomed, Inc. v. Lupin Pharms., Inc.*, 4:09-CV-05587. Pet. 1. In addition, Petitioner filed several petitions requesting *inter partes* review of related patents. *Id*. at 2. Those cases are: IPR2014-00651 (involving the '340 patent); IPR2014-00653 and IPR2014-00654 (involving U.S. Patent No. 6,340,475 B2); and IPR2014-00655 and IPR2014-00656 (involving U.S. Patent No. 6,635,340 B2). *Id.* We consolidated the oral hearings for the three instituted proceedings: IPR2014-00652, IPR2014-00654, and IPR2014-00656. *See* Paper 57.

C. The '340 Patent

The '340 patent relates to drugs formulated as unit oral dosage forms by incorporating them into matrices formed of a combination of poly(ethylene oxide) ("PEO") and hydroxypropyl methylcellulose ("HPMC"). Ex. 1001, Abstract. The matrices swell upon exposure to gastric fluid to a size large enough to promote retention (*id*. at Abstract, 11:66–67) and release the drugs into the stomach or upper gastrointestinal ("GI") tract, rather than the lower portions of the GI tract (*id*. at 1:10–13). The '340 patent discloses that when nutritive materials enter the stomach, the stomach is in "fed mode" and the pyloric sphincter is open partially. *Id*. at 1:62–2:9. During the "fed mode," particles exceeding about 1 cm in size are retained in the stomach, because they are too large to pass through a partially open pyloric sphincter. *Id*. at 2:5–11.

PEO and HPMC are both water-swellable polymers. *Id*. at 3:11–15, 3:23–25, 10:38–46, Fig. 5. According to the '340 patent, the swelling and controlled release properties of PEO are balanced with the predictable erosion behavior of HPMC, which modulates the extent and progress of the overall swelling of a combined polymeric matrix. *Id*. at 3:40–43. The '340 patent discloses that the competing, yet complementary, actions of swelling and erosion allow for slower and more even disintegration compared to tablets made solely or primarily with PEO. *Id*. at 3:50–54.

Certain embodiments in the specification of the '340 patent teach that for highly soluble drugs, the PEO component of the matrix limits the initial release of the drug while imparting gastric retention through swelling. *Id*. at 4:5–7. In other embodiments, the specification teaches that for sparingly soluble drugs, the HPMC component of the matrices prevents premature release of the drugs by retarding the erosion rate of the PEO, while the PEO provides gastric retention. *Id*. at 4:10–14.

The specification further teaches that prolonged release rates reduce the problem of transient overdosing, and control the dosage to safer and more effective levels over an extended period of time. *Id*. at 7:44–49.

D. Illustrative Claim

As noted above, an *inter partes* review was instituted as to claims 1, 3–5, and 10–13 of the '340 patent, of which claim 1 is the only independent claim. Claim 1 is illustrative of the challenged claims and is reproduced below (with paragraphing):

> 1. A controlled-release tablet for releasing a drug into at least a portion of a region defined by the stomach and the upper gastrointestinal tract, said tablet comprising a solid monolithic matrix with said drug dispersed therein,

> said matrix comprising a combination of poly(ethylene oxide) and hydroxypropyl methylcellulose at a weight ratio that causes said matrix to swell upon contact with gastric fluid to a size large enough to provide gastric retention,
> wherein said drug has a solubility in water that exceeds one part of said drug per ten parts of water, by weight, and
> wherein said poly(ethylene oxide) has a viscosity average molecular weight of from about 2,000,000 to about 10,000,000 daltons, and
> wherein said hydroxypropyl methylcellulose has a viscosity of from about 4,000 centipoise to about 200,000 centipoise, measured as a 2% solution in water.

Id. at 11:60–12:9.

II. DISCUSSION

A. Claim Construction

In an *inter partes* review, claim terms in an unexpired patent are interpreted according to their broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 42.100(b); *see also In re Cuozzo Speed Techs., LLC*, 793 F.3d 1268, 1278–79 (Fed. Cir. 2015) ("Congress implicitly approved the broadest reasonable interpretation standard in enacting the AIA," and "the standard was properly adopted by PTO regulation."), *reh'g en banc denied*, 793 F.3d 1297 (Fed. Cir. 2015). Under that standard, and absent any special definitions, we give claim terms their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007).

In the Decision to Institute, we construed the terms "monolithic matrix," "to swell upon contact with gastric fluid to a size large enough to provide gastric retention," and "gastric fluid" in independent claim 1. *See* Dec. to Inst. 6–10. During the course of the trial, neither party challenged

our constructions of these claim terms. PO Resp. 11–12. Thus, we see no reason to alter the constructions of these claim terms as set forth in the Decision to Institute, and we incorporate our previous analysis for purposes of this decision. Therefore, for the reasons set forth in the Decision to Institute, we interpret various claim terms of the '340 patent as follows:

Term(s)	Interpretation
"monolithic matrix"	"a matrix constructed as a single piece"
"to swell upon contact with gastric fluid to a size large enough to provide gastric retention"	"to increase in size upon contact with gastric fluid such that the tablet remains in the stomach"
"gastric fluid"	"both the fluid in the stomach and simulated or artificial fluids recognized by those skilled in the art as a suitable model for the fluid of the human stomach"

See Dec. to Inst. 6–10.

All other claim terms will be given their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention.

B. Principles of Law

To prevail in its challenges to the patentability of the claims, a petitioner must establish facts supporting its challenges by a preponderance of the evidence. 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d). A claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations, including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of skill in the art; and (4) objective evidence of nonobviousness, i.e., secondary considerations. *See Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

We analyze the instituted grounds of unpatentability in accordance with the above-stated principles.

C. Level of Ordinary Skill in the Art

In determining whether an invention would have been obvious at the time it was made, we consider the level of ordinary skill in the pertinent art at the time of the invention. *Graham*, 383 U.S. at 17. "The importance of resolving the level of ordinary skill in the art lies in the necessity of maintaining objectivity in the obviousness inquiry." *Ryko Mfg. Co. v. Nu-Star, Inc.*, 950 F.2d 714, 718 (Fed. Cir. 1991).

Petitioner contends that a person of ordinary skill in the art at the time of the '340 patent would have "at least a bachelor's degree in chemistry, chemical engineering, pharmaceutical science and/or material science, as well as substantial experience (for example, at least several years of industrial or academic work) in the design and/or development of controlled release oral drug dosage forms." Pet. 10 (citing Ex. 1008). Petitioner further contends that a person of ordinary skill in the art "would also need to possess, or have access to, the skill of a pharmacologist familiar with how such medicines work in the body." *Id.* According to Petitioner's declarant, Dr. Clive Wilson, a person of ordinary skill in the art "would have experience, or access to other persons with experience, in the field of

pharmacology, with particular emphasis on the pharmacokinetics and pharmacodynamics of oral drugs absorbed in the GI tract." Ex. 1008 ¶ 26.

Patent Owner does not disagree with Petitioner's assertion regarding the level of skill in the art, nor does Patent Owner offer its own explanation regarding who would qualify as a person of ordinary skill in the art relevant to the '340 patent offer. PO Resp. 11.

Based on our review of the '340 patent and the types of problems and solutions described in the '340 patent and cited prior art, we conclude a person of ordinary skill in the art at the time of the '340 patent would have a Bachelor's degree in chemistry or a similar discipline, and at least several years of work experience in the design and/or development of controlled release oral drug dosage forms. We further note that the applied prior art reflects the appropriate level of skill at the time of the claimed invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001).

D. Alleged Obviousness of Claims 1, 3–5, and 10–13 in View of the Shell 1998 Publication

Petitioner alleges that claims 1, 3–5, and 10–13 of the '340 patent are unpatentable under 35 U.S.C. § 103 in view of the Shell 1998 publication. Pet. 25–28. Patent Owner disputes Petitioner's position, arguing that although the Shell 1998 Publication discloses the use of both PEO and HPMC alone, it does not disclose, teach, or suggest the combination of PEO and HPMC as required by the challenged claims. PO Resp. 13. We have reviewed the Petition, the Patent Owner Response, and Petitioner's Reply, as well as the relevant evidence discussed in those papers. For reasons that follow, we determine that Petitioner has shown by a preponderance of the evidence that claims 1, 3–5, and 11–13 of the '340 patent are unpatentable in view of the Shell 1998 publication. We also determine Petitioner has not

shown by a preponderance of the evidence that claim 10 would have been obvious in view of the Shell 1998 publication.

1. Overview of the Shell 1998 Publication

The Shell 1998 Publication discloses drugs formulated as unit oral dosage forms by incorporating them into polymeric matrices that can be compressed into tablets. Ex. 1003, Abstract. The dosage forms are solid prior to administration to a patient, water-swellable, and gastric retentive in a fed mode (a state triggered by food ingestion that lasts for a period of time). *Id*. at 2:23–32, 3:2–5. The Shell 1998 Publication specifically discloses polymeric matrices made from (i) cellulose polymers and their derivatives, (ii) polysaccharides and their derivatives, (iii) polyaklylene oxides, and (iv) crosslinked polyacrylic acids and their derivatives. *Id*. at 5:4–6. Particularly preferred alkyl-substituted celluloses are hydroxyethylcellulose and HPMC. Ex. 1003, 5:17–18. A particularly preferred polyalkylene oxide is PEO. *Id*. at 5:22–23.

The Shell 1998 Publication further discloses that in terms of their viscosities, one class of preferred alkyl-substituted celluloses includes those whose viscosity is within the range of about 100 to about 110,000 centipoise as a 2% aqueous solution at 20°C, while another class includes those whose viscosity is within the range of about 1,000 to about 4,000 centipoise as a 1% aqueous solution at 20°C. *Id*. at 5:13–16. For PEO, the Shell 1998 Publication teaches that a preferred viscosity range is about 50 to about 2,000,000 centipoise for a 2% aqueous solution at 20°C. *Id*. at 5:26–28.

The Shell 1998 Publication teaches that the water-swellable polymers it discloses can be used individually or in combination with each other. *Id*. at 6:32. According to the Shell 1998 Publication, "[c]ertain combinations

will often provide a more controlled release of the drug than their components when used individually." *Id*. at 6:32–34. The Shell 1998 Publication gives examples of such combinations, including combining cellulose-based polymers with gums, such as hydroxyethyl cellulose or hydroxypropyl cellulose combined with xanthan gum, or combining PEO with xanthan gum. *Id*. at 6:34–36.

The polymer mixture can then be impregnated or combined with a drug and formed into particles, tablets, or retained in capsules. *Id*. at 7:3–4, 7:24–26. According to the Shell 1998 Publication, the disclosed invention applies to drugs that are "freely soluble" in water, meaning that one part of the drug dissolves in less than about ten parts water. *Id*. at 4:7–9. "The matrix itself is solid prior to administration and, once administered, remains undissolved in (*i.e*., uneroded by) the gastric fluid for a period of time sufficient to permit a majority of the drug to be released . . . ." *Id*. at 3:3–4.

2. Analysis

a. The Shell 1998 Publication Teaches or Suggests All the Recited Limitations of Independent Claim 1

Independent claim 1 requires a solid monolithic matrix made of PEO and HPMC with a drug dispersed in the matrix. Ex. 1001, 11:60–12:9. The claim characterizes PEO and HPMC by a specified viscosity and states that the drug must be water soluble. *Id.* The claim further recites that the weight ratio of the polymers in the matrix must cause the matrix to swell when the tablet gets to the stomach, so the tablet is retained in the stomach. *Id.*

According to Petitioner, the Shell 1998 Publication identifies a small number of preferred polymers, including "particularly preferred" polymers PEO and HPMC, used to create a solid polymeric matrix in which a drug is

dispersed. Pet. 25. Petitioner explains that the Shell 1998 Publication teaches the use of the polymers individually or in combination. *Id.*; *see* Ex. 1008 ¶ 83. For example, the Shell 1998 Publication discloses polymeric matrices made from combinations of PEO and hydroxyethyl cellulose. Pet. 25 (citing Ex. 1003, 12:13–16, 13:27–30). The Shell 1998 Publication also lists hydroxyethyl cellulose and HPMC as two "[p]articularly preferred alkyl-substituted celluloses" that can be used in the polymeric matrices. Ex. 1003, 5:17–18. Petitioner supports its position with the declaration of Dr. Clive Wilson, who testifies that based on the disclosure of the Shell 1998 Publication, it would have been obvious for a skilled artisan to use combinations of HPMC and PEO polymers to achieve a gastric retentive controlled-release dosage form as recited in challenged claim 1. Ex. 1008 ¶ 88. Petitioner, thus, concludes that the Shell 1998 Publication teaches or at least suggests the combination of PEO and HPMC for polymeric matrices and renders the challenged claims obvious. Pet. 28.

Patent Owner contests Petitioner's conclusion that the Shell 1998 Publication teaches or suggests a matrix made from a combination of PEO and HPMC as required by independent claim 1. PO Resp. 13. To the contrary, Patent Owner contends the Shell 1998 Publication does not disclose or contemplate a matrix comprising the combination of PEO and HPMC. *Id*. at 14. Patent Owner specifically argues that (1) the overwhelming majority of polymeric matrices taught by the Shell 1998 Publication are made of just one polymer, and (2) the combinations taught by the Shell 1998 Publication all use xantham gum or hydroxyethyl cellulose because these polymer combinations "provide a more controlled release of the drug than their components when used individually." PO Resp. 14

(citing Ex. 1003, 6:32–36, 12:13–16, 13:22–14:5). Patent Owner also contends that the Shell 1998 Publication does not include PEO and HPMC on a "short list" of polymers that could be combined to form a polymeric matrix. *Id.* at 18. Rather, Patent Owner argues that PEO and HPMC are on a "short list" to be used either independently or in combination with other polymers (such as xantham gum or hydroxyethyl cellulose) that did not meet certain performance criteria for controlled drug release. *Id.* According to Patent Owner, HPMC is not interchangeable with xantham gum or hydroxyethyl cellulose for the purposes of creating gastric retentive, controlled release tablets, because, as shown in Figure 6 of the Shell 1998 Publication, PEO and xantham gun were beneficial in a mixture with hydroxyethyl cellulose, whereas HPMC was not. *Id.* at 18–19 (citing Ex. 1003, Fig. 6); Ex. 2009 ¶ 70.

Patent Owner further contends that not only does the Shell 1998 Publication fail to disclose, suggest, or teach the exact combination of PEO and HPMC, but based on the Shell 1998 Publication, a person of ordinary skill in the art specifically would not have contemplated combining PEO and HPMC. PO Resp. 16; Ex. 2009 ¶ 58. Patent Owner contends that PEO and HPMC performed adequately on their own to control drug release, and there was no indication that combining PEO and HPMC would improve on their independent performance, or would have been "promising to try." *Id.* Patent Owner specifically argues that without first identifying a deficiency in the performance of individual polymers (*e.g.*, PEO and HPMC alone), a person of ordinary skill in the art would not have combined them, and even if a person of ordinary skill in the art would have combined the polymers, the behavior of the resultant mixture would not have been predictable. *Id.*

(citing Ex. 2009 ¶¶ 59–63). Patent Owner relies on the declaration of Dr. Hopfenberg to support its position. Dr. Hopfenberg testifies that:

> [C]ombining polymers introduces uncertainty related to the structure and properties of the combination of individual polymers comprising the combination. These structural variations can significantly affect the properties that are critical for a gastric-retentive controlled release form, including swelling, drug release, mechanical integrity, and the tendency to undergo long term degradation of the matrix of the dosage form subsequent to the designed release.

Ex. 2009 ¶ 59.

> The results set forth in Figure 6 of the Shell 1998 [publication] reveal that, with respect to drug retention in the dosage form after immersion for one hour, the behavior of the mixtures was unpredictable based on the behavior of the corresponding homopolymers . . . [t]he HEC/PEO and HEC/XG mixtures [used in the immersion experiment] showed significant improvement over HEC alone, yet the HEC/HPMC mixture, similar to HEC alone, failed to retain at least 40% of the drug after one hour. The dramatically different effect on drug retention following immersion resulting from forming an HEC combination with HPMC, as opposed to forming an HEC combination with PEO or XG, could not have been predicted.

Id. ¶ 63.

Thus, Patent Owner concludes that given the unpredictability of mixing two different polymers, a person of ordinary skill in the art would not set out to do so, absent a compelling motivation, and the Shell 1998 Publication provides no such motivation. PO Resp. 17–18 (citing Ex. 2009 ¶ 64).

We do not agree with Patent Owner, because an obviousness analysis "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and

creative steps that a person of ordinary skill in the art would employ." *KSR*, 550 U.S. at 418; *see In re Translogic Tech., Inc.*, 504 F.3d. at 1259. A combination would have been obvious under § 103 if "there are a finite number of identified, predictable solutions" to a known problem and when a path has been identified that "leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense." *KSR*, 550 U.S. at 418. The Court of Appeals for the Federal Circuit has elaborated that the identified path must "present a finite (and small in the context of the art) number of options easily traversed to show obviousness." *Ortho–McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358, 1364 (Fed.Cir. 2008).

Although the Shell 1998 Publication does not disclose a polymeric matrix made from a combination of PEO and HPMC, it does disclose a short list of polymers to be used individually in producing a solid matrix for controlled drug release, of which HPMC (Ex. 1003, 5:17–18) and PEO (*id.* at 5:22–23) are particularly preferred polymers. The Shell 1998 Publication also teaches that polymers can be combined to form a polymeric matrix. *Id.* at 6:32–34. The Shell 1998 Publication does not limit which polymers could be combined or suggest that certain polymers would not function properly in a combination matrix. *Id.*; *see In re Susi*, 440 F.2d 442, 445 (CCPA 1971) (affirming obviousness rejection where the disclosure of the prior art was "huge, but it undeniably include[d] at least some of the compounds recited in appellant's generic claims and it is of a class of chemicals to be used for the same purpose as appellant's additives"). Furthermore, we credit the testimony of Dr. Wilson, who stated that "as of October 2001, PEO and HPMC were widely known polymers in the art for use in controlled release

drug delivery systems" and "the Shell 1998 Publication identifies only a limited number of particularly preferred polymers, including PEO and HPMC." Ex. 1044 ¶ 28. Those facts support a conclusion that one would have understood that the Shell 1998 Publication "teaches that these polymers can be used in combination." *Id.* Thus, given the teachings in the Shell 1998 Publication, we determine that there were a finite number of identified, predictable polymers that could be used individually or in combination to create a solid matrix for controlled drug release and we further determine that the combination of PEO and HPMC, identified by the Shell 1998 Publication as particularly preferred polymers, would have been obvious to one of ordinary skill in the art at the time of the '340 patent. *KSR*, 550 U.S. at 421 (describing that a person of ordinary skill possesses "ordinary creativity, [and is] not an automaton").

Patent Owner, however, argues that even if a person of skill in the art would have contemplated a combination of PEO and HPMC in light of the Shell 1998 publication, there would not have been a reasonable expectation of success because it could not be predicted whether the disclosed polymer mixtures would have worked. PO Resp. 21 (citing Ex. 2009 ¶ 63). Yet, obviousness does not require absolute predictability. *Allergan, Inc. v. Apotex, Inc.*, 754 F.3d 952, 965 (Fed. Cir. 2014); *In re O'Farrell*, 853 F.2d 894, 903 (Fed.Cir.1988). What does matter is whether the prior art gives direction as to what parameters are critical and which of many possible choices may be successful. *Allergan*, 754 F.3d at 965. While success in employing the disclosed polymers to form a solid matrix for controlled drug release may not have been guaranteed, we are satisfied that explicitly identifying PEO and HPMC as particularly preferred polymers sufficiently

provided guidance as to what parameters and polymers would lead to a reasonable expectation of success.

Therefore, we determine that the Shell 1998 Publication at least suggests a polymeric matrix made from a combination of PEO and HPMC and, given the Shell 1998 Publication's teachings, we find that a person of ordinary skill in the art would have been able to make and use the claimed invention without anything more than routine experimentation. Accordingly, we hold that Petitioner has shown by a preponderance of the evidence that independent claim 1 is unpatentable under 35 U.S.C. § 103(a) for obviousness in view of the Shell 1998 Publication.

b. The Shell 1998 Publication Teaches or Suggests the Recited Limitations of Dependent Claims 3–5 and 11–13

Petitioner contends dependent claims 3–5 and 10–13 are unpatentable under 35 U.S.C. § 103(a) for obviousness over the Shell 1998 Publication. Pet. 27–28. Patent Owner contests Petitioner's position, arguing that the challenged dependent claims share the same material requirement of a PEO/HPMC combination as independent claim 1, and therefore, for the same reasons that claim 1 is not obvious over the Shell 1998 Publication, the dependent claims also are not obvious over the Shell 1998 Publication. PO Resp. 24. We agree with Petitioner's position, as supported by the testimony of Dr. Wilson, that the Shell 1998 Publication teaches the HPMC and PEO molecular weight and viscosities required by dependent claims 3 and 4 (Ex. 1003, 4:33–5:1, 5:13–15, 5:28–30), as well as the drug water solubility required by dependent claim 5 (*id.* at 4:9–12) and the proportions of the dosage form made up by the combination of PEO and HPMC required by dependent claims 11–13 (*id.* at Example 1, 8). *See* Ex. 1008 ¶¶ 82, 91, 125,

130, 131, 135, 141, 144, 147. Accordingly, we hold that Petitioner has shown by a preponderance of the evidence that dependent claims 3–5 and 11–13 are unpatentable under 35 U.S.C. § 103(a) for obviousness in view of the Shell 1998 Publication.

c. The Shell 1998 Publication Fails to Teach or Suggest the Recited Limitations of Dependent Claim 10

Petitioner contends dependent claim 10 is unpatentable under 35 U.S.C. § 103(a) for obviousness over the Shell 1998 Publication. Pet. 27–28. Patent Owner contests Petitioner's position, arguing that the challenged dependent claim 10 shares the same material requirement of a PEO/HPMC combination as independent claim 1, and therefore, for the same reasons that claim 1 is not obvious over the Shell 1998 Publication, claim 10 also is not obvious over the Shell 1998 publication. PO Resp. 24.

While we agree with Petitioner that the Shell 1998 Publication teaches or suggests the limitations of claims 1, 3–5, and 11–13, we are not satisfied that Petitioner has shown by a preponderance of the evidence that the Shell 1998 Publication teaches or suggests the PEO:HPMC weight ratio set forth in dependent claim 10. The testimony of Petitioner's declarant, Dr. Wilson, merely provides that the Shell 1998 Publication "disclose[s] a controlled-release dosage form dispersed in a water-swellable polymeric matrix, and that the polymers of the matrix, including PEO and HPMC, can be used individually or in combination." *See* Ex. 1008 ¶¶ 138, 140. Neither Petitioner nor Dr. Wilson provide an explanation of how the Shell 1998 Publication renders the specific PEO:HPMC weight ratios set forth in dependent claim 10 obvious. A determination of obviousness cannot be sustained by mere conclusory statements; instead, there must be some

articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. *KSR*, 550 U.S. at 418; *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006).

Furthermore, we must be careful not to allow hindsight reconstruction of references to reach the claimed invention without any explanation as to how or why the reference would produce the claimed invention. *Kinetic Concepts, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1342, 1368 (Fed. Cir. 2012) (quoting *Innogenetics, N.V. v. Abbott Labs.*, 512 F.3d 1363, 1374 n.3 (Fed. Cir. 2008)); *see also KSR*, 550 U.S. at 421 ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning.").

Accordingly, we hold that Petitioner has not shown by a preponderance of the evidence that dependent claim 10 is unpatentable under 35 U.S.C. § 103(a) for obviousness in view of the Shell 1998 Publication.

E. Alleged Obviousness of Claims 1, 3–5, and 10–13 in View of the Shell 1998 Publication and Papadimitriou

Petitioner contends claims 1, 3–5, and 10–13 of the '340 patent are unpatentable under 35 U.S.C. § 103 in view of the Shell 1998 Publication and Papadimitriou. Pet. 29–32. Patent Owner disputes Petitioner's position, arguing that that one of skill in the art would not have combined the Shell 1998 Publication and Papadimitriou. PO Resp. 24–34. We have reviewed the Petition, the Patent Owner Response, and Petitioner's Reply, as well as the relevant evidence discussed in those papers. For reasons that follow, we determine that Petitioner has shown by a preponderance of the evidence that

the challenged claims would have been obvious in view of the Shell 1998 Publication and Papadimitriou.

1. Overview of Papadimitriou

Papadimitriou discloses a sustained drug delivery system achieved "by the use of hydrophilic polymer excipients, which swell in the presence of water." Ex. 1007, 232. Papadimitriou examines the percolation threshold for polymeric matrices and the impact of varying the concentration of hydrophilic polymer excipients in the matrices on drug release rates from lattice-type matrices. *Id*. at 232–33. Papadimitriou teaches the use of HPMC and PEO as hydrophilic water-swellable polymers, alone or in combination. *Id*. at 233, Fig. 1. The polymers are compressed into tablets that have a diameter of 9 mm and a height of 8mm. *Id*. As shown in Figure 1 of Papadimitriou, reproduced below, a polymer matrix containing PEO and HPMC swelled by at least 40% of its original size within 30 minutes.

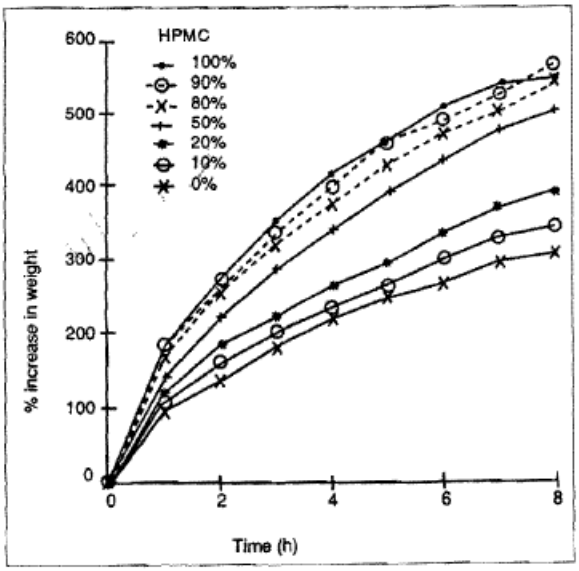

Figure 1 of Papadimitriou illustrates increases in weight (%) as a function of time for matrices composed of HPMC and/or PEO.

Based on the results indicated in Figure 1, Papadimitriou states "all the tablets were observed to swell significantly, as indicated by the large weight increase." Ex. 1007, 233.

Papadimitriou discloses PEO with a viscosity average molecular weight of from about 2,000,000 to 10,000,000 daltons. *Id*. at 233. Papadimitriou also discloses HPMC (i.e., Methocel K100M) with a viscosity in a range of approximately 4,000–200,000 centipoise, measured as a 2% solution in water. *Id*. at 233. Papadimitriou further discloses combinations of HPMC and PEO with ratios ranging from 100% HPMC:0% PEO to 0%HPMC:100%PEO. *Id*. at 233.

2. Overview of the Shell 1998 Publication

The disclosure of the Shell 1998 Publication is discussed in detail above in Section II.D.1.

3. Analysis

a. The Shell 1998 Publication and Papadimitriou Teach or Suggest All the Recited Limitations of Independent Claim 1

As discussed previously, independent claim 1 requires a solid monolithic matrix made of PEO and HPMC with a drug dispersed in the matrix. Ex. 1001, 11:60–12:9. Petitioner contends the Shell 1998 Publication in combination with Papadimitriou, as summarized above, teaches each limitation of claim 1. Pet. 28–31. Specifically, Petitioner argues that (1) the Shell 1998 Publication identifies a small number of preferred polymers, including "particularly preferred" polymers PEO and HPMC, that can be used individually or in combination to create a solid polymeric matrix in which a drug is dispersed, and (2) Papadimitriou likewise discloses a sustained drug delivery system achieved "by the use of

hydrophilic polymer excipients, which swell in the presence of water" and expressly teaches the use of HPMC and PEO as hydrophilic, water-swellable matrix polymers, alone or in combination. *Id.*; *see* Ex. 1008 ¶ 92 (citing Ex. 1003, 6:32; Ex. 1007, 232), ¶ 93 (citing Ex. 1007, 232, Fig. 1). Petitioner further notes that Papadimitriou specifically discloses Methocel K100M, a commercially available HPMC having a viscosity of 100,000 centipoise. Pet. 29; Ex. 1008 ¶¶ 93, 101.

According to Petitioner, a person of ordinary skill in the art would have been led to combine the teachings of the Shell 1998 Publication with Papadimitriou, because the disclosures share the common goal of releasing a drug in a controlled or sustained manner by using a swellable polymeric matrix. Pet. 30–31; *see* Ex. 1008 ¶ 94. Petitioner supports its position with the declaration of Dr. Wilson, who testifies that a skilled artisan "reading the Shell 1998 Publication would look to Papadimitriou for further examples of polymer matrices that would be compatible with the teachings of the Shell 1998 Publication." Ex. 1008 ¶ 94. Petitioner then concludes that the polymer matrix of Papadimitriou comprising a combination of HPMC and PEO can be used in the drug dosage form of the Shell 1998 Publication. Pet. 31; *see* Ex. 1008 ¶ 94.

Patent Owner disagrees with Petitioner's contention that one of ordinary skill in the art would look to combine the teachings of the Shell 1998 Publication and Papadimitriou. PO Resp. 24. First, Patent Owner argues that Papadimitriou does not disclose, teach, or suggest **any benefit** of the PEO/HPMC combination to any dosage form, let alone a gastric retentive one, but instead focuses on the unpredictable polymer-to-polymer interactions in such mixtures in order to underscore the **complexities and**

pitfalls of such polymer mixtures. *Id*. at 26; Ex. 2009 ¶ 74. Patent Owner then argues "[Petitioner] concedes that Papadimitriou does not teach or suggest gastric retentive drug dosage forms at all" because Petitioner's claim charts do not cite to Papadimitriou in relation to gastric retention. PO Resp. 28 (citing Pet. 20–21).

Second, Patent Owner argues that a person of ordinary skill in the art would not have combined Papadimitriou with the Shell 1998 Publication, because Papadimitriou is not related to gastric retention, which was an essential component of the problem solved by the '340 patent. *Id*. at 28. Patent Owner supports its argument that Papadimitriou is not directed to a gastric retentive dosage form with the fact that the swelling experiments in Papadimitriou were conducted at a neutral pH of 7.4, instead of an acidic pH similar to that of gastric fluid. *Id*. at 28–29 (citing Ex. 1007, 233); Ex. 2009 ¶ 79. Patent Owner then argues that Papadimitriou's experiments are deficient because Papadimitriou did not present any drug release profiles, and in fact, did not even include drug in any experiment. *Id.* at 30 (citing Ex. 1007, 233 ("In this work, the degree of swelling of combinations of the two excipients alone (i.e. **without drug** or other excipients) is considered.")) (emphasis added); Ex. 2009 ¶ 80. According to Patent Owner, the presence of drug would further impact how the polymers swelled. PO Resp. 30. Patent Owner further argues that the assays reported in Papadimitriou were carried out in phosphate buffer, which was known to be problematic for PEO because it leads to phase separation. *Id.* (citing Ex. 2009 ¶ 81; Ex. 2015 ¶ 29). Patent Owner relies on the testimony of Dr. Hopfenberg, whose testimony reiterates Patent Owner's contentions regarding the teachings in Papadimitriou. Ex. 2009 ¶¶ 74–87. Based on the postulated problems with

the experimental designs disclosed in Papadimitriou, Patent Owner asserts that a skill artisan would not rely on Papadimitriou in the creation of a controlled release dosage form, let alone a gastric retentive one. *Id*. at 30.

Lastly, Patent Owner argues that the combination of the Shell 1998 Publication and Papadimitriou would not have provided a person of ordinary skill in the art with a reasonable expectation of success in practicing the '340 patent claims. *Id*. at 31. According to Patent Owner, (i) a person of ordinary skill in the art would not have found the teachings of the Shell 1998 Publication and Papadimitriou compatible or directed to similar issues (*id*. at 31), and (ii) the unpredictable interactions of polymers as disclosed by Papadimitriou indicates that a person of ordinary skill "could not predict whether the disclosed xantham-based and HEC-based polymer combinations would work, as reflected by 'failed' combinations such as HEC/HPMC" (*id*. at 32–33 (citing Ex. 2009 ¶ 63)). Thus, Patent Owner concludes that a combination of the Shell 1998 Publication and Papadimitriou is based on impermissible hindsight because a skilled artisan would not have combined the teachings of the two references. *Id*. at 33.

Despite Patent Owner's arguments, we agree with Petitioner that challenged claims 1, 3–5, and 10–13 would have been obvious over the Shell 1998 Publication and Papadimitriou. Specifically, we find that a skilled artisan would look to the teachings of Papadimitriou in combination with the Shell 1998 Publication's disclosure in attempts to solve the problem of releasing a drug in a controlled or sustained manner by using a combination of PEO and HPMC, both of which are swellable hydrophilic polymers. This finding is based on the fact that Papadimitriou's disclosure is directed specifically to "sustained drug delivery . . . by the use of

hydrophilic polymeric excipients" (Ex. 1007, 232), while the Shell 1998 Publication is directed to sustained release unit dosage forms incorporated into polymeric matrices made of hydrophilic polymers (Ex. 1003, Abstract). *See id.* at 2:30–32, 3:8–11, 6:32–34; Ex. 1007, Abstract, 233; *see also* Ex. 1008 ¶ 92 ("[T]he Shell 1998 patent publication discloses that the water-swellable polymer matrix in which the drug is dispersed may be formed of an individual polymer or a combination of polymers (Exh. 1003, 6:32) . . . Papadimitriou expressly teaches the use of HPMC and PEO as hydrophilic, water-swellable matrix polymers, alone or in combination. (Exh. 1007, p. 233, Fig. 1).") Therefore, contrary to Patent Owner's statements, the references are directed to similar issues and disclose PEO and HPMC as swellable hydrophilic polymers. Accordingly, we hold that a skilled artisan at the time of the invention would have considered the teachings of Papadimitriou compatible with the teachings of the Shell 1998 Publication, and would apply the disclosures in combination.

We also are not persuaded by Patent Owner's arguments, as they narrowly focus on small differences between Papadimitriou and the Shell 1998 Publication and fail to consider the collective teachings of Papadimitriou and the Shell 1998 Publication from the perspective of one of ordinary skill in the art. *See KSR*, 550 U.S. at 420 ("[F]amiliar items may have obvious uses beyond their primary purpose, and in many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle.") The fact that Papadimitriou uses PEO and HPMC, which are called out specifically in the Shell 1998 Publication as particularly preferred polymers to use, weighs in favor of finding that a person of ordinary skill in the art would "fit the teachings" of Papadimitriou and the

Shell 1998 Publication together to render the challenged claims obvious. Additionally, the arguments presented by Patent Owner appear to attack Papadimitriou individually, rather than in combination with the Shell 1998 Publication. *See* PO Resp. 26–30. Nonobviousness cannot be established by attacking the references individually when a challenge is predicated upon a combination of prior art disclosures. *See In re Merck & Co., Inc.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986). In attacking Papadimitriou individually, Patent Owner fails to address Petitioner's actual challenges or, therefore, establish an insufficiency in the combined teachings of the references.

Furthermore, we are not persuaded by Patent Owner's arguments that the combination of the Shell 1998 Publication and Papadimitriou would not have provided a person of ordinary skill in the art with a reasonable expectation of success in practicing the '340 patent claims because the nature of polymer mixtures is unpredictable. The case law is clear that obviousness cannot be avoided simply by showing some degree of unpredictability in the art, as long as there was a reasonable probability of success. *See Pfizer, Inc. v. Apotex*, 480 F.3d 1348, 1369 (Fed. Cir. 2007); (holding that "a skilled artisan would have had a reasonable expectation of success with the besylate salt form of amlodipine at the time the invention was made"); *In re Corkill*, 771 F.2d 1496, 1500 (Fed. Cir. 1985) ("Although [the inventor] declared that it cannot be predicted how any candidate will work in a detergent composition, but that it must be tested, this does not overcome [the prior art's] teaching that hydrated zeolites will work.").

This is not a case where the prior art merely teaches to pursue a "general approach that seemed to be a promising field of experimentation" or "gave only general guidance as to the particular form of the claimed

invention or how to achieve it." *O'Farrell*, 853 F.2d at 903 ("Obviousness does not require absolute predictability of success . . . [A]ll that is required is a reasonable expectation of success."); *Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1165 (Fed.Cir.2006) ("While the definition of 'reasonable expectation' is somewhat vague, our case law makes clear that it does not require a *certainty* of success.") (internal citations omitted). Although success in employing the disclosed polymers to form a solid matrix for controlled drug release may not have been guaranteed, we are satisfied that the Shell 1998 Publication in view of Papadimitriou sufficiently provided guidance as to what parameters and polymers would lead to a reasonable expectation of success by explicitly identifying PEO and HPMC as particularly preferred polymers.

Accordingly, we hold that Petitioner has shown by a preponderance of the evidence that independent claim 1 is unpatentable under 35 U.S.C. § 103(a) for obviousness in view of the Shell 1998 Publication and Papadimitriou.

b. The Shell 1998 Publication and Papadimitriou Teach or Suggest the Recited Limitations of Dependent Claims 3–5 and 10–13

Petitioner contends dependent claims 3–5 and 10–13are unpatentable under 35 U.S.C. § 103(a) for obviousness over the Shell 1998 Publication and Papadimitriou. Pet. 31–32. Patent Owner contests Petitioner's position, arguing that the challenged dependent claims share the same material requirement of PEO/HPMC combinations as independent claim 1, and therefore, for the same reasons that claim 1 is not obvious over the Shell 1998 Publication and Papadimitriou, the dependent claims also are not

obvious over the Shell 1998 Publication and Papadimitriou. PO Resp. 34. For reasons stated above, we find that position unpersuasive.

We agree with Petitioner's further position, as supported by the testimony of Dr. Wilson, that the Shell 1998 Publication and Papadimitriou teach (a) the HPMC and PEO molecular weight and viscosities required by dependent claims 3 and 4 (Ex. 1003, 4:33–5:1, 5:13–15, 5:28–30), (b) the drug water solubility required by dependent claim 5 (*id.* at 4:9–12), (c) the weight ratio of PEO to HPMC as required by dependent claim 10 (Ex. 1007, 233), and (d) the proportions of the dosage form made up by the combination of PEO and HPMC required by dependent claims 11–13 (Ex. 1003, Example 1, 8). *See* Ex. 1008 ¶¶ 91, 92, 127, 128, 133–137, 139, 141–149. Accordingly, we hold that Petitioner has shown by a preponderance of the evidence that dependent claims 3–5 and 10–13 are unpatentable under 35 U.S.C. § 103(a) for obviousness in view of the Shell 1998 Publication.

F. Alleged Obviousness of Claims 1, 3–5, and 10–13 in View of Edgren and Papadimitriou

Petitioner contends claims 1, 3–5, and 10–13 of the '340 patent are unpatentable under 35 U.S.C. § 103 in view of Edgren and Papadimitriou. Pet. 39–42. Patent Owner disputes Petitioner's position, arguing that one of skill in the art would not have had reason to combine Edgren and Papadimitriou. PO Resp. 34–42. We have reviewed the Petition, the Patent Owner Response, and Petitioner's Reply, as well as the relevant evidence discussed in those papers. For reasons that follow, we determine that Petitioner has not shown by a preponderance of the evidence that the challenged claims are unpatentable as obvious over Edgren and Papadimitriou.

1. Overview of Edgren

Edgren describes a controlled-release dosage form for delivering a drug in the gastrointestinal tract comprising a beneficial drug and at least two different cellulose ethers (*i.e.*, a polymer matrix) that swell when hydrated. Ex. 1006, 1:12–13, 2:37–52; 3:17, 11:23–28. Edgren further discloses that its polymeric matrices are composed of a low number average molecular weight HPMC and a high number average molecular weight HPMC. *Id*. at Abstract, 5:10–26, 11:23–28. The drugs disclosed in Edgren include those that are very soluble, such as captopril and ranitidine. *Id*. at 2:53–56, 2:61–68, 5:27–67, 8:47; 9:1–2. Edgren describes a drug dosage form comprising at least thirty weight percent of HPMC polymers and up to seventy weight percent of a soluble drug. *Id*. at 1:17–19, 1:30–32, 3:8–10. According to Edgren, the drug/HPMC mixture can be fed into a hopper of a compression machine, where about two tons of pressure is applied to compress the composition together into a dosage form. *Id*. at 7:27–31.

Edgren teaches that the disclosed HPMC polymers make "available a drug delivery matrix suitable for retention in the stomach for gastric retention over the drug releasing life time of the dosage system." *Id*. at 10:65–68. Edgren further teaches that the HPMC polymers swell extensively when hydrated and reduce irritation of mucosal tissue by the drug because there is less direct drug contact with the tissue. *Id*. at 11:23–28.

2. Overview of Papadimitriou

The disclosure of Papadimitriou is discussed in detail above in Section II.E.2.

3. Analysis

Petitioner contends Edgren, as summarized above, in combination with Papadimitriou teaches or suggests each limitation of claims 1–5 and 10–13 of the '340 patent. Pet. 39–42. Petitioner specifically contends that Edgren teaches the use of polymeric ethers in combination and does not teach away from using PEO with HPMC. Reply 8. Petitioner supports its position with a declaration of Dr. Wilson, who testifies that the "Background of the Invention" section of Edgren describes disadvantages of prior art formulations that used HPMC with other cellulosic ethers, however, none of the prior art cited in Edgren used PEO. Ex. 1044 ¶ 63. Dr. Wilson, therefore, opines that Edgren cannot be considered as teaching away from using polymers, such as PEO and HPMC, in combination. *Id.* ¶ 64.

Petitioner also contends that a person of ordinary skill in the art would have been led to combine the teachings of Edgren with Papadimitriou, because the disclosures share the common goal of releasing a drug in a controlled or sustained manner by using a swellable polymeric matrix. *Id.* at 40–41; *see* Ex. 1008 ¶¶ 115–116. According to Petitioner, a skilled artisan reading Edgren would look to Papadimitriou for further examples of polymer matrices that would be compatible with the teachings of Edgren. Petitioner then contends that one of the goals of Edgren was to provide greater mechanical integrity than the dosage forms of the prior art, and PEO, as disclosed in Papadimitriou, was a readily available polymer with high swelling potential that was known to increase mechanical integrity. Reply 9 (citing Ex. 1043 ¶ 65; Ex. 1006, 1:27–44, 3:1–7, 11:3–7; Ex. 2023, 145:4–149:2). Petitioner concludes that because it was known that polymers could be combined to provide better controlled release (*see, e.g.*, Ex. 1003), it

would have been obvious to a skilled artisan that the polymer matrix of Papadimitriou, comprising a combination of HPMC and PEO, could have been used in the drug dosage form of Edgren. Pet. 41; Reply 9 (citing Ex. 1043 ¶ 65).

Patent Owner disagrees with Petitioner's contention, arguing the claim would not have been obvious in view of the combination of Edgren and Papadimitriou, for several reasons. PO Resp. 34–41. First, Patent Owner argues that a skilled artisan would not have combined Edgren with Papadimitriou because Edgren teaches away from the claimed PEO/HPMC combination. *Id.* at 35. According to Patent Owner, Edgren specifically discourages combining HPMC with polymeric ethers (of which PEO is a member). *Id.* Second, Patent Owner argues there is no reason why a skilled artisan would have thought to combine the elements of Edgren and Papadimitriou, because (i) Edgren is directed to combining two forms of HPMC, (ii) Edgren does not disclose PEO, (iii) PEO and HPMCs are not interchangeable, (iv) Papadimitriou – and its disclosure of a PEO/HPMC combination – does not apply to gastric retentive dosage form, and (v) reading Edgren and Papadimitriou together would not provide a skilled artisan with a reasonable expectation that the unique PEO/HPMC combination of the'340 patent would work for the intended purpose of providing gastric retention and controlled drug release. *Id.* at 37–39; *see* Ex. 2009 ¶¶ 92–93.

On the record developed at trial, we are not persuaded that Petitioner has shown by a preponderance of the evidence that a person of ordinary skill in the art would have had a reason to combine the references with a reasonable expectation of success. Although the references may have

interrelated teachings because they both are directed to polymers, Petitioner has not explained persuasively *how or why* a person of ordinary skill in the art would have exchanged one of the HPMCs in the Edgren formulation with PEO in the formulation of Papadimitriou.

Edgren specifically discloses using "at least two cellulose ethers that function together for enhancing the pharmaco-release kinetics of the dosage form" and using a "cellulose ether formulation [of high molecular weight HPMC and low molecular weight HPMC that] operate[s] as a unit in a moving fluid for controlling the rate of release of a beneficial drug from the dosage form." Ex. 1006, 2:33–45. Despite this disclosure, Petitioner argues that a skilled artisan would have used PEO in the Edgren formulation simply because "PEO was a readily available polymer with high swelling potential that was known to increase mechanical integrity." *See* Reply 9; Ex. 1043 ¶ 65. Petitioner provides insufficient evidence that a person of skill in the art would have found PEO (a non-cellulose ether) to be interchangeable with low molecular weight HPMC (a cellulose ether) or that PEO would have been able to act as a unit with high molecular weight HPMC as described in Edgren. In fact, at deposition, Petitioner's declarant, Dr. Wilson, testified that PEOs and low molecular weight HPMCs are not interchangeable.

> Q. Is it your position that all of the Polyoxes that make up the class of Polyoxes and all of the low molecular weight HPMCs that make up that class are interchangeable in terms of their ability to absorb water?
>
> A. No.
>
> Q. They are not interchangeable?
>
> A. They are not interchangeable.
> You would get a different characteristic
> but then you would blend backwards and

> forwards to get the required uptake of water you are seeking.
>
> Q. So there are differences amongst the various Polyox and low molecular weight HPMCs in terms of their ability to absorb water, correct?
>
> A. Yes, there is, yes.
>
> Q. And there are, likewise, differences in terms of their ability to swell?
>
> A. Yes.
>
> Q. And in terms of their ability to erode, correct?
>
> A. That's true.

Ex. 2023, 279:21–280:21.

Given this testimony, we find that Petitioner's argument is fraught with hindsight bias. *See KSR*, 550 U.S. at 418 ("A patent composed of several elements is not proved obvious by merely demonstrating that each of its elements was, independently, known in the prior art."); *Kinetic Concepts, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1342, 1368–69 (Fed. Cir. 2012) ("[Smith & Nephew] never offered evidence articulating why a person having ordinary skill in the art would combine the primary references to obtain the disclosed inventions."); *Innogenetics, N.V. v. Abbott Labs.*, 512 F.3d 1363, 1373–74 (Fed. Cir. 2008) ("We must still be careful not to allow hindsight reconstruction of references to reach the claimed invention without any explanation as to how or why the references would be combined to produce the claimed invention."). In the absence of PEO and low molecular weight HPMC being readily interchangeable, Petitioner needed to explain what would have led a person of ordinary skill in the art at the time of the invention to replace low molecular weight HPMC in the Edgren formulation with PEO. Petitioner failed to provide such an explanation.

Petitioner must demonstrate obviousness by a preponderance of the evidence. *See Yamaha Int'l Corp. v. Hoshino Gakki Co.*, 840 F.2d 1572, 1580 n.11 (Fed. Cir. 1988) (stating that the ultimate burden of persuasion [to establish a fact by a preponderance of the evidence] is only critical in the situation where the evidence is so evenly balanced that no preponderance emerges. In that event, the party having the burden of persuasion necessarily loses.). After considering the parties' arguments and evidence, however, we are not persuaded that Petitioner has made a sufficient showing that a person of ordinary skill would have combined the teachings in the manner contended by Petitioner. Accordingly, we hold that Petitioner has not shown by a preponderance of the evidence that independent claim 1 is unpatentable under 35 U.S.C. § 103(a) for obviousness in view of Edgren and Papadimitriou. For the same reasons, we are hold Petitioner has failed to establish the unpatentability of dependent claims 3–5 and 10–13 by a preponderance of the evidence.

G. Secondary Considerations of Non-Obviousness

Factual inquiries for an obviousness determination include secondary considerations based on evaluation and crediting of objective evidence of nonobviousness. *See Graham*, 383 U.S. at 17. Notwithstanding what the teachings of the prior art would have suggested to one of ordinary skill in the art at the time of the invention, the totality of the evidence submitted, including objective evidence of nonobviousness, may lead to a conclusion that the challenged claims would not have been obvious to one of ordinary skill in the art. *In re Piasecki*, 745 F.2d 1468, 1471–72 (Fed. Cir. 1984). Secondary considerations may include any of the following: long-felt but unsolved needs, failure of others, unexpected results, commercial success,

copying, licensing, and praise. *See Graham*, 383 U.S. at 17; *Leapfrog Enters., Inc. v. Fisher-Price, Inc.*, 485 F.3d 1157, 1162 (Fed. Cir. 2007).

To be relevant, evidence of nonobviousness must be commensurate in scope with the claimed invention. *In re Kao*, 639 F.3d 1057, 1068 (Fed. Cir. 2011) (citing *In re Tiffin*, 448 F.2d 791, 792 (CCPA 1971)); *In re Hiniker Co.*, 150 F.3d 1362, 1369 (Fed. Cir. 1998). In that regard, in order to be accorded substantial weight, there must be a nexus between the merits of the claimed invention and the evidence of secondary considerations. *In re GPAC Inc.*, 57 F.3d 1573, 1580 (Fed. Cir. 1995). "Nexus" is a legally and factually sufficient connection between the objective evidence and the claimed invention, such that the objective evidence should be considered in determining nonobviousness. *Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387, 1392 (Fed. Cir. 1988). The burden of showing that there is a nexus lies with the patent owner. *Id.*; *see Paulsen*, 30 F.3d at 1482. Here, Patent Owner argues that commercial success, licensing, long-felt but unresolved need, unexpected results, and the length of time it took to invent the challenged claims indicates that the claims would not have been obvious to a person of ordinary skill in the art. PO Resp. 43–55.

1. Commercial Success

Patent Owner argues that it has successfully commercialized the patented inventions in multiple drugs on the market. PO Resp. 49. As its example, Patent Owner cites the drug Gralise® and its sales and market share data. *Id.* at 50–51. As explained above, evidence of commercial success is "only significant if there is a nexus between the claimed invention and the commercial success." *Ormco Corp. v. Align Tech., Inc.*, 463 F.3d 1299, 1311–12 (Fed. Cir. 2006). To establish a nexus between a claimed

invention and the commercial success of a product, there must be "proof that the sales [of the allegedly successful product] were a direct result of the unique characteristics of the claimed invention—as opposed to other economic and commercial factors unrelated to the quality of the patented subject matter." *See In re GPAC, Inc.*, 57 F.3d 1573, 1580 (Fed. Cir. 1995) ("For objective evidence to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the claimed invention."); *Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387, 1392 (Fed. Cir. 1988), *cert. denied* (1988) ("A prima facie case of nexus is generally made out when the patentee shows both that there is commercial success, and that the thing (product or method) that is commercially successful is the invention disclosed and claimed in the patent."); *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1539 (Fed. Cir. 1983) (holding that patent owner failed to show nexus between the merits of the invention and the commercial success of a tubing product). On the record before us, we are not persuaded that the evidence shows sufficiently a nexus between any success of Patent Owner's products and the invention claimed in the '340 patent.

Specifically, Patent Owner has not shown sufficiently in its Patent Owner Response that Gralise® embodies the claims of the '340 patent. Instead, Patent Owner cites its declarant, Dr. Hopfenberg, and claim charts, stating only that Dr. Hopfenberg "opines that there is a direct nexus between the '340 patented technology and the Gralise® product." PO Resp. 49 (citing Ex. 2009 ¶¶ 96–97). Patent Owner then states that "[b]y claim charts, he finds that the Gralise® product embodies each and every limitation of the claims of the '340 Patent." *Id.* at 49–50 (citing Ex. 2009 ¶ 97 (citing Ex.

2011, a 9-page claim chart)). We determine that merely citing to a claim chart as support—without any explanation in the Patent Owner Response—is insufficient to demonstrate a nexus and violates our rule against incorporation by reference.[6] *See* 37 C.F.R. § 42.6(a)(3) ("Arguments must not be incorporated by reference from one document into another document.").

Accordingly, absent an adequate demonstration of nexus in the Petition, we give little weight to Patent Owner's argument that the alleged commercial success of Gralise® is evidence that the claims are not obvious.

2. Licensing

Patent Owner also argues that its licensing program establishes that the claims are not obvious. PO Resp. 51. Patent Owner asserts that it has "entered into 10 different license agreements (two of them with one licensee) since 2002 for the '340 patented technology (known as the Acuform® technology)." *Id.* at 51–52. Patent Owner further asserts that its licenses have "generated substantial upfront, milestone, and royalty payments for [Patent Owner]." *Id.* at 52. Patent Owner concludes that "[t]he fact that so many different third parties have acknowledged [Patent Owner's] patented technology and voluntarily made substantial payments for licenses to the '340 patented technology is strong evidence that the patented inventions were [not] obvious at their time." *Id.* at 52–53.

[6] We recognize the challenge of fully addressing the nexus issue within our default page limits. We note, however, that Patent Owner did not request additional pages for its Response or even attempt to address at least a single claim in the Response.

We are not persuaded. As with evidence of commercial success, "only little weight can be attributed to such evidence if the patentee does not demonstrate a nexus between the merits of the invention and the licenses of record." *In re GPAC Inc.*, 57 F.3d 1573, 1580 (Fed. Cir. 1995) (citation omitted). Moreover, our reviewing court has held that "without a showing of a nexus, 'the mere existence of . . . licenses is insufficient to overcome the conclusion of obviousness.'" *In re Antor Media Corp.*, 689 F.3d 1282, 1293 (Fed. Cir. 2012) (quoting *Iron Grip Barbell Co. v. USA Sports, Inc.*, 392 F.3d 1317, 1324 (Fed. Cir. 2004)).

Like the applicant in *Antor Media*, Patent Owner has done little more than list the licenses and their respective sales revenue. *See id.* at 1293–94. The cited testimony of Dr. Nicholson only details the revenues for each license and does not establish whether the licensing program was successful because of the merits of the claimed invention or for other economic reasons, such as to avoid litigation or because of prior business relationships. *See* Ex. 2014 ¶¶ 46, 77; *see also Antor Media*, 689 F.3d at 1294 (affirming Board's finding that evidence of existence of licenses was insufficient to overcome prima facie case of obviousness).

Accordingly, we give little weight to Patent Owner's argument that its licensing program is evidence that the claims are not obvious.

3. Long-Felt but Unsolved Need

Patent Owner argues that Dr. Berner (inventor of the '340 patent) "provides credible information that there was a long-felt need for a once daily, gastric-retentive, controlled-release dosage form to deliver highly soluble drugs slowly, evenly, and reproducibly." PO Resp. 53 (citing Ex. 2009 ¶¶ 98–99). Patent Owner also describes the use of the drugs

Metformin and gabapentin to reduce side-effects and increase patient-compliance of prior art drugs. *Id.* at 53–54.

We are not persuaded. Patent Owner must show that any evidence of long-felt need "demonstrates both that a demand existed for the patented invention, and that others tried but failed to satisfy that demand." *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1082 (Fed. Cir. 2012). Patent Owner's argument is lacking as to the latter element. That is, Patent Owner offers no evidence that others tried and failed.

Accordingly, we give little weight to Patent Owner's argument that there was a long-felt but unmet need that overcomes Petitioner's showing of obviousness in this case.

4. Undue Experimentation and Unexpected Results

Patent Owner argues that the '340 patent claims would not have been obvious because it took the inventors one and a half years of extensive experimentation to first recognize the "unexpectedly beneficial performance" of PEO and HPMC for gastric retention and controlled drug release. PO Resp. 44 (citing Ex. 2014 ¶ 24). According to Patent Owner, "anything-but-'routine experimentation' was necessary" to conceive of the claimed inventions in the '340 Patent. *Id.* (citing Ex. 2014 ¶ 27). We find this argument unpersuasive in light of Exhibits 2018 and 2019. As Petitioner notes, PEO was used by scientists (working on a project for Patent Owner) on the first day of the project, January 21, 1999 (Ex. 2018, 138), and HPMC was suggested for use in the formulation on February 17, 1999 (*id.* at. 180). We cannot pinpoint the exact date of invention for the '340 patent claims, because we are limited to the evidence of record. Given the record

that is available to us, we are not persuaded the inventors of the '340 patent took "approximately one and a half years of extensive experimentation" to conceive the '340 patent. The lengthy experiments performed in Exhibits 2018 and 2019 do not show lack of invention, because it appears Patent Owner undertook that work to satisfy particular commercial requirements. *See CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1340 (Fed. Cir. 2003) ("In general, few patented inventions are an immediate commercial success. Rather, most inventions require further development to achieve commercial success.").

Accordingly, we give little weight to Patent Owner's argument that the evidence of alleged unexpected results overcomes Petitioner's showing of obviousness in this case.

III. MOTIONS TO EXCLUDE EVIDENCE AND MOTION FOR OBSERVATIONS REGARDING DEPOSITION TESTIMONY

Both parties filed motions to exclude evidence offered by the other side. The party moving to exclude evidence bears the burden of proving that it is entitled to the relief requested—namely, that the material sought to be excluded is inadmissible under the Federal Rules of Evidence. *See* 37 C.F.R. §§ 42.20(c), 42.62(a). We address each party's motion in turn.

A. Petitioner's Motion to Exclude Evidence

Petitioner filed a Motion to Exclude Evidence seeking to exclude Exhibits 2163 and 2164, which were introduced during the deposition of Petitioner's Declarant, Dr. Wilson. Paper 51 ("Mot."). Even without excluding this evidence, we have determined that Petitioner has established, based on a preponderance of the evidence, the unpatentability of claims 1, 3–5, and 10–13 of the '340 patent. Furthermore, Petitioner's arguments on

these items go to the weight to be accorded to the evidence. The Board is capable of determining and assigning the appropriate weight to the evidence.

For these reasons, we *deny* Petitioner's motion.

B. Patent Owner's Motion to Exclude

Patent Owner filed a Motion to Exclude Evidence seeking to exclude Exhibits 1030 and 1031 as constituting inadmissible new prior art. PO Mot. Exclude. Patent Owner further seeks to exclude Exhibit 1021 as irrelevant and prejudicial. *Id.* at 1. Petitioner opposes Patent Owner's Motion, arguing that (1) Exhibits 1030 and 1031 were submitted with Petitioner's Reply as proper rebuttal evidence to arguments made Patent Owner's Response, and (2) the Office Patent Trial Practice Guide (77 Fed. Reg. 48,756, 48,764 (Aug. 14, 2012)) allows a Petitioner to attach claim charts from another proceeding to its Petition (such as Exhibit 1021). Pet. Exclude Opp., 1.

Patent Owner's arguments on these items go to the weight to be accorded to the evidence. It is within our discretion to assign the appropriate weight to be accorded to evidence. *See, e.g.*, *Yorkey v. Diab*, 601 F.3d 1279, 1284 (Fed. Cir. 2010) (holding the Board has discretion to give more weight to one item of evidence over another "unless no reasonable trier of fact could have done so"); *In re Am. Acad. of Sci. Tech Ctr.*, 367 F.3d 1359, 1368 (Fed. Cir. 2004) ("[T]he Board is entitled to weigh the declarations and conclude that the lack of factual corroboration warrants discounting the opinions expressed in the declarations."); *Velander v. Garner*, 348 F.3d 1359, 1371 (Fed. Cir. 2003) ("In giving more weight to prior publications than to subsequent conclusory statements by experts, the Board acted well within [its] discretion."). The Board is capable of determining and assigning the appropriate weight to the evidence.

For this reason, we *deny* Patent Owner's Motion to Exclude Exhibits 1030 and 1031.

Additionally, on this record, we need not decide Patent Owner's Motion regarding Ex. 1021, because our analysis does not rely upon the information in that particular exhibit. Consequently, Patent Owner's Motion to Exclude Exhibit 1021 is dismissed as moot.

IV. CONCLUSION

We conclude Petitioner has shown by a preponderance of the evidence that claims 1, 3–5, and 10–13 of the '340 patent are unpatentable under 35 U.S.C. § 103(a) for obviousness over (1) the Shell 1998 publication, and (2) the Shell 1998 Publication in view of Papadimitriou.

Petitioner's Motion to Exclude Exhibits 2163 and 2164 is denied. Patent Owner's Motion to Exclude Exhibit 1021 is dismissed, and Patent Owner's Motion to Exclude Exhibits 1030 and 1031 is denied.

V. ORDER

For the reasons given, it is

ORDERED that, by a preponderance of the evidence, claims 1, 3–5, and 10–13 of the '340 patent are unpatentable;

FURTHER ORDERED that Petitioner's Motion to Exclude Exhibits 2163 and 2164 is denied;

FURTHER ORDERED that Patent Owner's Motion to Exclude Exhibit 1021 is dismissed;

FURTHER ORDERED that Patent Owner's Motion to Exclude Exhibits 1030 and 1031 is denied;

FURTHER ORDERED that because this is a Final Written Decision, parties to the proceeding seeking judicial review of the decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

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CERTIFICATE OF SERVICE

I, Arlene L. Chow, hereby certify that on this 29th day of April, 2016, I caused the foregoing brief to be filed electronically with the Clerk of the Court for the United States Court of Appeals for the Federal Circuit by using the appellate CM/ECF system. Participants in this case who are registered CM/ECF users will be served by the appellate CM/ECF system. I further certify that all of the participants in this case are registered CM/ECF users.

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CERTIFICATE OF COMPLIANCE

I, Arlene L. Chow, hereby certify, pursuant to Federal Circuit Rule 28(a)(14), that the foregoing brief complies with the type-volume limitation described in Federal Rule of Appellate Procedure 32(a)(7)(B). The brief was prepared in Microsoft Word, is proportionally spaced, has a typeface of Times New Roman, 14-point, and contains 11,208 words, excluding those sections identified in Federal Rule of Appellate Procedure 32(a)(7)(B)(iii) and Federal Circuit Rule 32(b).

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